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(54) Title: SULFINYL HEXOSE DERIVATIVES USEFUL FOR GLYCOSYLATION

Glycosyl Donor   Glycosyl Acceptor   Resin

Acyl Group
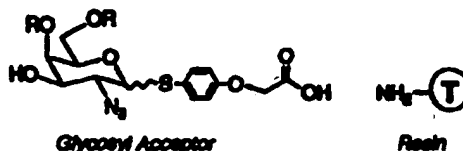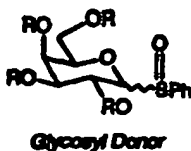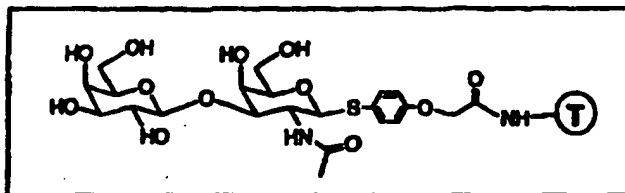
(57) Abstract

Hexose derivatives are described which facilitate control over the stereochemistry of the glycosyl bond formed in the course of a solid phase glycosylation reaction. Methods for their use are also described.

SULFINYL HEXOSE DERIVATIVES USEFUL FOR GLYCOSYLATION

1. FIELD OF THE INVENTION

The present invention relates to the field of
carbohydrate synthesis. It provides a set of hexose
derivatives which are characterized by their ability to
glycosylate, under appropriate conditions, a wide range
of substrates in high chemical yield and with high
stereoselectivity. The compounds of the invention are
useful for the synthesis of carbohydrates and other
glycosylated materials, and are especially suitable for
the synthesis of carbohydrates on polymeric supports.
In particular, they are suitable for the synthesis of
carbohydrate libraries by parallel or combinatorial
methods.

2. BACKGROUND

Oligosaccharides and polysaccharides, as
components of glycoproteins and glycolipids, are
ubiquitous on cell surfaces where they function as
cell-surface markers that protein receptors can
recognize. Although such carbohydrate-mediated cell-
cell interactions are of importance in many biological
events, our understanding of the structure-function
relationships has been very slow to develop because of
the difficulty of synthesizing well-defined
oligosaccharides for study.

Carbohydrate ligands play central roles in a wide
variety of normal and abnormal biological recognition
processes. Among their less benign roles,
carbohydrates on cell surfaces have been implicated in
chronic inflammation, in viral and bacterial infection,

and in tumorigenesis and metastasis. Strategies to
block the interactions between cell surface
carbohydrates and their protein receptors could provide
an effective means of preventing or treating various
diseases. Antibodies directed to either the
carbohydrate ligands or to their respective receptors
represent one approach; another strategy is to deploy
ligands which bind to the protein targets better than
the natural cell surface carbohydrates. Consequently,
there is great potential for, and a great amount of
research into, the use of synthetic oligosaccharides as
therapeutic agents.

One application of synthetic oligosaccharides is
for the inhibition of cell adhesion. For example, a
critical step in the inflammatory response is the
adhesion of circulating neutrophils to the endothelial
lining of blood vessels, which is an essential
precursor to neutrophil infiltration of the surrounding
tissue. The neutrophils initially adhere via
carbohydrate ligands to adhesion molecules (selectins)
and then, in the presence of pro-inflammatory
chemokines, they bind more tightly via a family of cell
adhesion molecules (CAMs) called integrins. The
integrins incorporate carbohydrate ligands that bind to
intracellular adhesion molecules (ICAMs) on the
epithelium. There is currently great interest in
synthetic carbohydrate ligands that might interfere
with selectin and/or integrin binding; such agents are
expected to be of use in the treatment of asthma, ARDS,
reperfusion injury, multiple sclerosis, and various
other chronic inflammatory diseases.

Another example of this application of synthetic
carbohydrates is the inhibition of bacterial adhesion
to human tissue. Many pathogenic bacteria adhere to
carbohydrate ligands on the host cells, and this
adhesion can be blocked by the appropriate synthetic

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oligosaccharide. For many bacteria, colonization is impossible without adhesion, and carbohydrate-based therapies for several infectious diseases, such as *H. pylori*-induced ulcers and pneumonia, are currently being developed.

Certain oligosaccharides are of utility for the induction of immune responses, for antibody production, as vaccines, or to induce disease states in research animals. For example, the trisaccharide nephritogenoside is used to induce glomerulonephritis in animals, and has received the attention of synthetic chemists for some time: H. Zhang, Y. Wang, W. Voelter, *Tetrahedron Lett.*, **36**, 1243-1246 (1995) and references therein.

Despite the promise of synthetic oligosaccharides for research and therapeutic applications, there is at present no universally applicable method for the synthesis of these complex molecules. Enzymatic methods have been developed recently which are quite effective for the regiospecific and stereospecific formation of glycosidic linkages, but the enzymes are fairly specific for particular substrates and not widely applicable to the variety of structures one would like to synthesize. See: O. Karthaus et al, *J. Chem. Soc. Perkin Trans. 1*, 1851-1857 (1994); M Schuster, P. Wang, J. Paulson, C.-H. Wong, *J. Amer. Chem. Soc.*, **116**, 1135 (1994); and references therein.

Chemical synthesis is not limited in this fashion, and in principle is capable of providing any desired oligosaccharide, and therefore carbohydrate synthesis has become a very active field of research. Novel glycosylation reactions and clever strategies for carbohydrate synthesis have been developed. Some fairly complex oligosaccharides have been synthesized, but to date there is no generally applicable "universal" method that can reliably generate

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glycosidic linkages with control of regiochemistry and
stereochemistry. Subtle changes in the structures of
glycosyl donors and acceptors change the regiochemical
and stereochemical outcomes, and on the yields, of
existing glycosylation reactions. Consequently, every
oligosaccharide synthesis is a unique undertaking.
This state of affairs does not permit the synthesis of
large libraries of oligosaccharides for screening
purposes. The application of combinatorial methods of
synthesis requires especially reliable chemistry, and
the combinatorial synthesis of oligosaccharide
libraries is therefore well beyond the reach of present
methods.

Thus, although the power of combinatorial
synthesis for identifying drug leads and elucidating
structure-activity relationships may have been
appreciated for some time in specific areas of drug
discovery, the combinatorial approach has not been
successfully applied to the synthesis and screening of
carbohydrate-based ligands, including, for example,
polysaccharides and glycoconjugates. In contrast,
methods to make peptides and nucleic acids on solid
supports have been available for many years and so it
is not surprising that the first combinatorial
libraries involved peptides and nucleic acids. In
contrast, methods to synthesize carbohydrates on the
solid phase are only now being developed. The reliable
preparation of a combinatorial oligosaccharide library
requires consistently high-yielding reactions, which
give well-defined products from a variety of substrates
under standardized reaction conditions.

A related requirement is the availability of a set
of stable carbohydrate monomers that are suitable for
these reactions. These monomers should not only add to
the growing oligosaccharide chain in high yield, but
should carry suitable protecting groups that can be

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selectively removed to enable attachment of the next
monomer unit. Similar requirements apply to the
incorporation of carbohydrate monomer units into non-
oligosaccharide libraries (e.g., glycopeptides or
glycoproteins). Such a set of monomers would, of
course, be useful for solid-phase or solution-phase
synthesis of individual simple and complex
carbohydrates, as well.

Synthesis of combinatorial libraries, especially
on solid supports, puts great demands on the chemistry
employed. Each step in a multi-step combinatorial
library synthesis should provide the desired product
with high yield, otherwise the final yield of the
expected products drops to low levels. The number of
by-products rises to unacceptable levels, after several
rounds of synthesis. Even with yields at the level of
90% per reaction, the maximum amount of product that
can be expected after only five consecutive reactions
is 59%, 35% after ten such reactions. Moreover, such
90% or better yields must be obtained simultaneously,
under the same reaction conditions, for the enormous
number of different monomer/oligomer combinations that
are present in a growing library.

There is a great need, therefore, for a method of
linking saccharide monomers that can be relied on to
generate regiochemically and stereochemically well
defined products in high yield. Such a method would
allow research workers other than skilled synthetic
chemists to engage in the preparation of
oligosaccharides. Likewise, there is a need for a
synthetic methodology that is reliable enough to be
carried out using automated equipment, analogous to the
automated DNA and automated peptide synthesizers that
are a mainstay of nucleic acid, protein chemistry and
combinatorial library synthesis research. Both of
these needs would be met by a reliable method of solid-

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phase oligosaccharide synthesis that approaches the
kinds of results obtained using techniques currently
available for peptides and nucleic acids.

2.1.   Existing Methods of Oligosaccharide Synthesis

The requirements of the field of solid-
phase oligosaccharide synthesis have been evident to
the workers in the field of carbohydrate synthesis and
much effort has, in fact, been invested in the
development of various approaches with mixed results.

For instance, Schuerch et al., in *Carbohydrate
Res.* (1972) 22:399-412, utilized glycosyl bromides as
glycosyl donors to form glycosidic linkages to a
polymer-supported glycosyl acceptor. However, the
solid-phase reactions were much slower than the
analogous solution-phase glycosylations. Consequently,
the highly reactive and unstable glycosyl bromides
underwent side reactions and eventual decomposition.
Moreover, stereocontrol by C6 substituents, observed in
solution, did not translate well to the solid-phase
reactions. Thus, stereocontrol of the glycosidic
linkages was also poor.

Gagnaire et al., in *Tetrahedron Lett.* (1972) 5065,
attempted to catalyze polymer-supported glycosylation
by D-glycosyl bromides with mercuric ions. They did
achieve the preparation of beta(1→6) linkages on the
solid phase by means of neighboring-group
participation. They could not, however, obtain the
alpha anomers cleanly unless the glycosyl acceptors
were sterically hindered, and these hindered acceptors
reduced the yield to about 55%.

Because of the additional difficulties presented
by the poor transferability of solution-phase methods
to solid-phase carbohydrate synthesis, some efforts to

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make carbohydrate libraries have involved the synthesis of mixtures of carbohydrates in solution.

In one attempt to eliminate the problems introduced by the solid-phase support, Guthrie et al. utilized a soluble polystyrene resin as a "solid" support together with an orthoester glycosylation method to obtain moderate yields of disaccharides (R. Guthrie, A. Jenkins, G. Roberts, *J. Chem. Soc. Perkin Trans. 1*, 2414 (1973)). Later, Krepinsky et al. improved on this method by utilizing a soluble polyethylene glycol polymer, and by using a glycosyl trichloroacetimidate as the glycosyl donor (S. Douglas, D. Whitfield, J. Krepinsky, *J. Amer. Chem. Soc.*, 113, 5095 (1991)). Both Guthrie and Krepinsky attempted to retain one of the advantages of solid-phase synthesis, which is the ability to wash away spent and/or excess reagents. Both methods, therefore, require precipitation of the soluble polymer by addition of specific non-solvents. The precipitation steps must be repeated several times at each step of the synthesis, resulting in substantial material losses. In addition, the precipitation steps make automation problematic and add greatly to the time required to complete a synthesis.

A further limitation imposed by soluble "solid" supports is the fact that, when used for the synthesis of carbohydrate libraries, they do not generally permit resolution; that is, the soluble supports, even when in precipitated form, do not allow the physical separation or segregation and subsequent identification of individual members (e.g., single beads) of the library. Indeed,, the library obtained from such soluble supports is a mixture at the molecular level. Therefore, in most cases, deconvolution is the only available technique for identifying library members that are of interest. There thus remains a need for a method of

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preparing carbohydrate libraries that are particularly
amenable to resolution strategies, such as chemical
tagging or spatial addressing methods or direct
structure determination of product removed from the
solid or polymer support.

Kahne et al. (D. Kahne, S. Walker, Y. Cheng, D.
van Engen, J. Amer. Chem. Soc., 111, 6881-6882 (1989);
S. Kim, D. Augeri, D. Yang, D. Kahne, J. Amer. Chem.
Soc., 116, 1766-1775 (1994)) have described a
sulfoxide-mediated glycosylation reaction that is high-
yielding and reliable, in terms of being applicable to
a variety of substrate combinations. These authors
have applied this method to solid-phase synthesis of
specific oligosaccharides. L. Yan, C. Taylor, R.
Goodnow, D. Kahne, J. Amer. Chem. Soc., 116, 6953-6954
(1994); D. Kahne, PCT Int. Appl. Publication No. WO
94/19360 (1994). Still, where the 1,2-cis isomers of
oligosaccharide products are desired, the degree of
stereochemical control was found to be inadequate.
Synthetic Oligosaccharides (ACS Symposium Series 560,
1994) p. 158.

Where the 1,2-trans isomers of glycosylation
products are desired, it is well-known that they may be
obtained selectively when a neighboring group at C-2
participates in the glycosylation. This process is
illustrated in Scheme 1 (below), where a 2-α-acyloxy
group (a typical participating group) on an L-glucosyl
sulfoxide is shown to form a cyclic cationic
intermediate, which directs the incoming acceptor to
the β position. As mentioned, above, where 1,2-cis
isomers are desired, however, the presence of a non-
participating C-2 substituent is insufficient to assure
"clean" production of the 1,2-cis isomer.
Consequently, unless the acceptor is sterically
hindered, mixtures of products cis and trans isomers
are usually obtained.

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This problem of lack of stereochemical control in
the case of 1,2-cis linkages has been documented by
others using sulfinyl glycosides as starting
substrates: Y. Wang, H. Zhang and W. Voelter obtained
a 2:1 α:β (cis:trans) ratio in the 6-O-glycosylation of
a glucose derivative with compound III (stereochemistry
= D-glucose, Ar = phenyl, all X = O, all G = benzyl)
(Z. Naturforsch. 48b, 1143-1145 (1993)), and also a 2:1
ratio in the glycosylation of a disaccharide with the
same donor (Z. Naturforsch. 50b, 661-666 (1995)). The
same authors later reported a 4:1 α:β ratio for the
former reaction (Tetrahedron Lett. 36, 1243-1246
(1995)). This glycosyl donor, when equipped with a C-2
participating group (III, stereochemistry = D-glucose,
Ar = phenyl, all X = O, all G = benzoyl), gave
exclusively the β (1,2-trans) anomer in a C-2
glycosylation reaction (T. Bamhaoud, J.-M. Lancelin,
J.-M. Beau, J. Chem. Soc. Chem. Commun., 1494-1496
(1992)) and, also, in a series of 6-glycosylation
reactions (L. Sliedregt, G. van der Marel, J. van Boom,
Tetrahedron Lett., 35, 4015-4018 (1994)). The latter
authors obtained similar results with galactose-derived
donors. A similar donor III with a non-participating
group at C-2 (stereochemistry = D-galactose, Ar =
phenyl, all X = O, all G = benzyl) did give 1,2-cis
products cleanly when glycosylating galactose
derivatives at C-3 and C-4; it should be noted,
however, that the starting substrates constitute
examples of hindered acceptors (A. Sarkar, K. Matta,
Carbohydr. Res., 233, 245-250 (1992)).

In the course of preparing the calicheamicin
trisaccharide, the glycosyl donor, shown below, lacking
a participating C-2 group, was reported to provide the
α-anomer with 12:1 selectivity. In this particular
case, however, the observed selectivity resulted from
the equilibration of an initially formed product

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mixture. Thus, the stereoselectivity of the reaction
itself is not high: S.-H. Kim, D. Augeri, D. Yang, D.
Kahne, *J. Amer. Chem. Soc.* **116**, 1766-1775 (1994).

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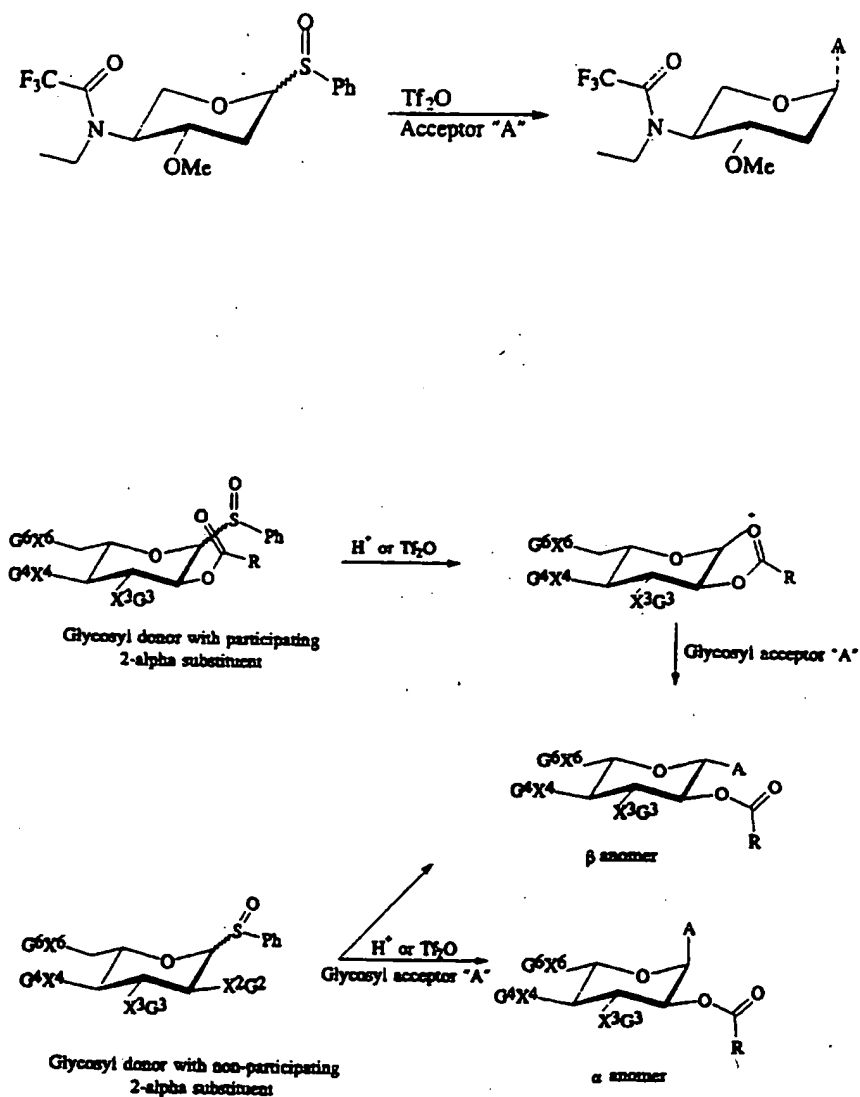
SCHEME I

The biological activity of oligosaccharides is sensitive to the stereochemistry of glycosidic linkages, and, from a biochemical, phramaclogic and pharmaceutical perspective, the alpha and beta anomers of a carbohydrate are considered entirely different substances. Thus, a reaction providing a 50:50 mixture

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of anomers, even if it proceeds in 100% *chemical* yield,
generates at best a 50% *stereochemical* yield of a
single compound. As noted above, a reliable 90% or
better yield at each step is minimally required for a
practical multi-step library synthesis. As the number
of synthetic steps rises, the required yield per step
also preferably rises. The instant discussion makes it
clear that no adequate methods exist in the present
state of the art for the reliable construction of
glycosidic linkages that present a 1,2-*cis* geometry,
especially in the context of library synthesis, where
the simultaneous α- or β-glycosylation of multiple
types of starting substrates is desired.

Thus, the need for reliable methods of
glycosylation, which provide good chemical yields and
good stereochemical control with a wide variety of
substrates, remains unmet by the state of the art. In
particular, there remains a need for classes of
glycosyl donors that provide 1,2-*cis* stereochemistry in
the carbohydrate product with good chemical yields and
stereochemical control, especially with unhindered
acceptors.

3. SUMMARY OF THE INVENTION

Accordingly, the present invention is directed to
certain carbohydrate monomers suitable for use in the
sulfoxide-mediated glycosylation reaction to provide
good chemical and stereochemical yields of desired
glycosylation products. In particular, carbohydrate
monomers are provided, which are capable of serving as
specialized glycosyl donors that can bias the
stereochemical outcome of a glycosylation reaction. In
a preferred embodiment of the present invention, the
resulting glycosidic linkage between the glycosyl donor
and glycosyl acceptor is such that the glycosidic ring
of the donor group bears substituents on the 1- and 2-

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positions in a cis relationship (specifically, the α anomer illustrated in Scheme I, above).

According to the present invention, a method is described which provides chemical and stereochemical yields of 90% or greater in favor of the 1,2-cis arrangement of substituents about the glycosidic ring of the reaction product obtained from the sulfoxide-mediated glycosylation reaction between an activated carbohydrate monomer, as disclosed herein, and most glycosyl acceptors.

It has been discovered that the carbohydrate monomers disclosed are useful, thus, as reagents for the synthesis of individual glycosidic moieties, whether composed substantially of one or more types of sugars or comprising glycoconjugates of varying degrees of complexity. It has further been discovered that these reagents are also useful in the preparation of carbohydrate or glycoconjugate libraries, particularly combinatorial libraries. It a preferred embodiment of the present invention, a method is described for the solid-phase synthesis of such libraries. In each case described above, the transformations leading to the glycosylation products proceed with high chemical yield. Most importantly, the stereochemical outcome of the transformations are carried out with a very high degree of control even in the absence of a participating neighboring group at the 2-position of the glycosyl donor.

Thus, the present invention is also directed to a method of controlling the stereochemical outcome of a glycosylation reaction in which a 1,2-cis configuration is formed between an acceptor attached via a glycosidic linkage to the 1-position of a glycosyl donor and a non-participating substituent at the 2-position of such glycosyl donor comprising contacting an acceptor with a glycosyl donor having (i) a non-participating

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substituent at the 2-position, (ii) a cyclic structure comprising the glycosidic carbons of either the 3- and 4-positions of the glycosyl donor and one or more substituents or the 4- and 6-positions of the glycosyl donor and one or more substituents, and (iii) a leaving group at the 1-position. In particular, embodiments of the invention the leaving group comprises a sulfoxide group, preferably an activated sulfoxide group and the non-participating substituent at the 2-position comprises a 2-alpha substituent. Moreover, the preferred stereochemical outcome provides a glycosidic linkage that defines the alpha anomer.

These and other objectives of the present invention, will be apparent to those of ordinary skill on consideration of the disclosure provided herein, particularly the following detailed description of the preferred embodiments.

4. DEFINITIONS

For the purposes of this disclosure, the following terms are defined as follows:

A *monosaccharide* refers to a pentose, hexose, heptose, or octose sugar, analog, or derivative thereof, including, but not limited to, deoxy sugars, dideoxy sugars, amino sugars and sugar acids. These terms include the protected and unprotected forms thereof (that is, in which selected reactive groups, typically oxygen- or nitrogen-bearing groups, of the carbohydrate monomer or monosaccharide have been either temporarily blocked to prevent their undergoing a reaction under the conditions of a specific transformation or left exposed and available for possible participation in a reaction, respectively).

Thus, a *protecting group* is any chemical moiety that is temporarily attached to a reactive functional group of a given molecule to mask the functional

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groups's reactivity while chemical reactions are permitted to proceed elsewhere on the molecule. Protecting groups preferred for protecting the reactive functional groups of sugars include, but are not limited to, alkyl, benzyl, acyl and silyl protecting groups. Many other s are well known to those of ordinary skill.

A *carbohydrate monomer* is a type of monosaccharide which is capable of influencing the stereochemical course of a glycosylation reaction such that the resulting glycosylation product bears substantially the stereochemistry desired (e.g., a 1,2-*cis* relationship among the substituents on the 1- and 2-positions of the glycosidic ring). A carbohydrate monomer is particular type of *glycosyl donor*, as defined below.

A *carbohydrate, disaccharide, oligosaccharide*, or *polysaccharide* each refers to a molecule or a portion thereof, which is comprised of two or more monosaccharides that are joined by a glycosidic linkage. A *sugar* is any carbohydrate, disaccharide, oligosaccharide, polysaccharide, or monosaccharide.

The term *carbohydrate-based ligand* refers to a substance having an affinity for a given receptor, such as a carbohydrate-binding protein or an enzyme, and is composed solely or partially of carbohydrate moieties. The term *carbohydrate ligand* may be used interchangeably with *carbohydrate-based ligand* in this disclosure.

A *low-affinity* ligand is one that, in solution, binds to a receptor with a dissociation constant of from about one hundred micromolar to about one hundred millimolar.

A *glycoconjugate* refers to any molecule, substance, or substrate, including a solid, that includes a monosaccharide, carbohydrate, disaccharide, oligosaccharide, or polysaccharide covalently attached

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or adhered to a non-sugar chemical, biochemical,
biological, or inorganic moiety. Preferred
glycoconjugates include, but are not limited to, small
molecules conjugated to the sugar (e.g.,
heteropolyaromatic-sugar conjugates, nucleosides,
nucleoside analogs and the like), glycopeptide,
glycoproteins and the like.

A *glycosyl donor* is a sugar with a leaving group
(or potential leaving group) on at least one of its
anomeric carbon which, under appropriate conditions, is
capable of participating in a glycosylation reaction by
which such anomeric carbon becomes covalently attached
to a second moiety, typically a *glycosyl acceptor*, as
defined below, or a nucleophile.

A *glycosyl acceptor* is any moiety, including a
sugar, having the capacity to participate as the second
moiety in the above-mentioned glycosylation reaction by
virtue of a nucleophilic (or potentially nucleophilic)
group present among the groups or substituents of such
moiety, such that a covalent bond is formed between the
anomeric carbon of such glycosyl donor and such
nucleophilic (or potentially nucleophilic) group.

The phrase "sulfoxide-mediated glycosylation
reaction" refers to the glycosylation technique first
described by Kahne *et al.* in *J. Am. Chem. Soc.* (1989)
111:6881.

The terms "lower alkyl," "lower alkoxy," "lower
acyloxy," or "lower alkenyl" refer to such
substituents, as the case may be, having one to five
carbon atoms, in either a linear or branched
arrangement. The term "aryl" refers to aromatic
groups, such as phenyl rings, naphthyl rings and the
like, optionally bearing one or more substituents on
the various ring positions. The term "heterocycle"
refers to five-membered or six-membered aromatic rings
containing one or more nitrogen, oxygen, or sulfur

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atoms, optionally bearing one or more substituents on the various ring positions. Such optional "substituents" may be any substituent that is chemically compatible with the aryl or heterocyclic ring and with the overall molecule of which such aryl or heterocyclic ring may be a part. Various aryl and heterocyclic rings may also be referred to herein as "substituted or unsubstituted" phenyl, naphthyl and the like to designate whether or not an optional substituent is present, respectively.

A *multivalent support* is any material or macromolecule to which more than one carbohydrate ligand can be attached, and includes, but is not limited to, organic dendrimers and polymers, glasses, metals and metal oxides, in any physical form such as solutions, emulsions, suspensions, beads, fibers, or planar surfaces.

The *detection* of a substance refers to the qualitative determination that the substance is present and may also refer to the quantitative measurement of the amount of the substance present. Detection may be by any means, including but not limited to affinity-based, physical, optical, radiometric, photometric, electrochemical, or spectroscopic methods. All such detection methods are intended to be within the scope of the present invention. There are a variety of detection methods known in the art, and it is well within the capacity of the skilled practitioner to choose the method most appropriate or convenient for each situation.

The *selection* of a particular ligand-probe interaction refers to the process of selectively recognizing the interaction of interest from among a potentially large number of possible interactions. The selection step includes, but is not limited to, the detection of the desired interaction. For instance,

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selection may include the selective resolution of one
or a few beads from a vessel filled with different
beads or one or two wells from a multi-well plate.

A *detectable moiety* is any particle, molecule,
fragment of a molecule, or atom whose presence and
concentration can be readily measured, preferably by
automated analytical instruments. The detectable
moieties include, but are not limited to, radioactive
isotopes, fluorescent molecules, chemiluminescent
compounds, chromophores, high-affinity ligands or
antigens, haptens, colloidal metal, enzymes, or other
species or catalysts that can either produce or be
manipulated to provide detectable products.

5. BRIEF DESCRIPTION OF THE FIGURES

Fig. 1 illustrates the synthetic scheme for the
preparation of compounds 1-20.

Fig. 2 illustrates the synthetic scheme for the
preparation of compounds 21-D-26.

Fig. 3 illustrates the synthetic scheme for the
preparation of compounds 27-33.

Fig. 4 illustrates the synthetic scheme for the
preparation of compounds 34-L-45.

Fig. 5 illustrates the synthetic scheme for the
preparation of compounds 46-53.

Fig. 6 illustrates the synthetic scheme for the
preparation of compounds 54-66.

Fig. 7 illustrates the synthetic scheme for the
preparation of compounds 67-77.

Fig. 8 illustrates the synthetic scheme for the
preparation of compounds 78-88.

Fig. 9 illustrates the synthetic scheme for the
preparation of compounds 81-95.

Fig. 10 illustrates, in a particular embodiment,
the building blocks that may make up a resin-bound
glycoside (depicted in the box). Using the particular

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hexose derivatives described herein as part of the available building blocks, one can prepare libraries having preferred stereochemistries.

6.   DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The invention in its broadest aspect provides a selection of protected 1-deoxy-1-(arylsulfinyl) hexose derivatives (glycosyl donors) of structures 1, 2, and 3 that are suitable for use in preparing glycosides with high stereoselectivity and in high yield. The compounds of the invention are especially suitable for the synthesis of glycosides and glycoside libraries on soluble polymeric supports, insoluble polymeric supports, and other solid-phase supports. Representative glycosides, one a donor and the other a potentially resin-bound acceptor, are depicted in Figure 10. Combining the various components give rise to a potential carbohydrate ligand bound to a solid phase support.

1   2   3
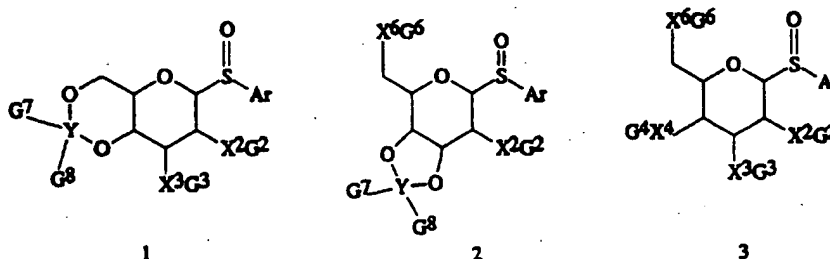
In the structures 1, 2, and 3, the groups X^2 through X^6 may be oxygen, and where X is oxygen the attached groups G^2 through G^6 may be:

C1 to C8 branched or unbranched alkyl or alkenyl (optionally substituted by one or more lower alkoxy, lower acyloxy, halogen, or aryl);

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C1 to C8 branched or unbranched acyl (optionally substituted by one or more lower alkoxy, lower acyloxy, halogen, or aryl);

benzoyl, optionally substituted by one or more lower alkyl, lower alkoxy, lower acyloxy, halogen, nitro, or aryl;

lower alkoxycarbonyl, optionally substituted by one or more lower alkenyl, lower alkoxy, lower acyloxy, halogen, aryl, or 9-fluorenyl; or

silicon, substituted by one or more lower alkyl, lower alkoxy, or aryl.

The groups X^2 through X^6 may each independently be nitrogen, and where X is nitrogen the attached group G may be:

C1 to C8 branched or unbranched acyl (optionally substituted by one or more lower alkoxy, lower acyloxy, halogen, or aryl);

benzoyl, optionally substituted by one or more lower alkyl, lower alkoxy, lower acyloxy, halogen, nitro, or aryl; or

lower alkoxycarbonyl, optionally substituted by one or more lower alkenyl, lower alkoxy, lower acyloxy, halogen, aryl, or 9-fluorenyl.

The groups X^2 through X^6 may further each independently be azido or hydrogen, and where X is azido or hydrogen the attached group G is not present.

The atom Y may be carbon, in which case the groups G^7 and G^8 are independently branched or unbranched lower alkyl, aryl, or hydrogen, or taken together G^7 and G^8 are a carbonyl oxygen doubly bonded to Y. The atom Y may also be silicon, in which case the groups G^7 and G^8 are independently branched or unbranched lower alkyl, lower alkoxy, or aryl.

The group Ar may be phenyl, naphthyl, or a heterocycle, all of which may be optionally substituted. For examples of the preparation and

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utility of substituted 1-(phenylsulfenyl)hexose
derivatives, see L. Sliedregt, G. van der Marel, J. van
Boom, Tetrahedron Lett., 35, 4015-4018 (1994). Ar is
preferably phenyl, 4-nitrophenyl, or 4-methoxyphenyl,
and is most preferably phenyl.

The preferred structures are 1 and 2, most
preferably 2. Where X^2 is oxygen, G^2 is preferably C1
to C8 branched or unbranched alkyl or alkenyl
(optionally substituted by one or more lower alkoxy,
lower acyloxy, halogen, or aryl); or C1 to C8 branched
or unbranched acyl (optionally substituted by one or
more lower alkoxy, lower acyloxy, halogen, or aryl).
Where X^2 is oxygen, G^2 is most preferably tertiary
alkyl, pivaloyl, or C1 to C3 alkyl substituted with one
or more aryl. Where any of X^3 through X^6 are oxygen,
the attached groups G^3 through G^6 are preferably chosen
from among the following: acetyl, pivaloyl, 2-
methoxyethyl, 2-(methoxy)ethoxymethyl, benzyl, 4-
methoxybenzyl, and trimethylsilyl. *Where Y is carbon,
the groups G^7 and G^8 preferably together form a
carbonyl oxygen.*

Most specifically, the invention provides
derivatives of D- and L-galactose, D- and L-mannose,
and D- and L-allose, and the 6-deoxy derivatives
thereof, which are suitable for the above applications.

It will be evident to those skilled in the art
that the sulfur atom in the compounds of the invention
is a chiral center, and that it may exist in mirror-
image configurations. This gives rise to
diastereomeric mixtures of sulfoxides, given the
chirality at C-1 of the hexoses; these diastereomers
may be separable by standard chromatographic methods or
by enzymatic methods (O. Karthaus, S. Shoda, S.
Kobayashi, Tetrahedron: Asymmetry 5 (11) 2213-2216
(1994). The compounds of the invention may also exist

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as alpha- or beta-anomers at the anomeric (C-1) carbon,
hence four diastereomers of each illustrated structure
are possible. All four diastereomers, and mixtures
thereof, are of approximately equal utility for the
preparation of glycosides. All four diastereomers,
individually and as mixtures, are thus contemplated by
the present invention. Furthermore, it will be evident
to those skilled in the art that these hexose
derivatives can be synthesized to generate glycosidic
libraries, initially bound but cleavable from polymeric
supports, as depicted in Figure 10.

7. EXAMPLES

The scope of the present invention is not limited
in any way by the scope of the examples provided below,
which are presented for illustrative purposes only.

7.1. Preparation of 1,6-Dideoxy-2,3,4-tri-O-pivaloyl-1-(phenylsulfinyl)-β-L-galactopyranose (5)

To a solution of L-fucose (1.03 g, 6.09
mmol) in 60 mL of pyridine at room temperature is added
acetic anhydride (4.6 mL, 4.96 g, 48.7 mmol). The
solution is stirred at room temperature for 20 h and
concentrated *in vacuo*. The residue is then dissolved
in 50 mL of CH_2Cl_2 and washed with 5% HCl (4 x 60 mL),
dried over anhydrous Na_2SO_4 and concentrated to afford
1.76 g (85%) of L-fucose tetraacetate 1 as a white
foam, a 5:2 (α:β) mixture of anomers: R_f 0.38 (40%
petroleum ether/EtOAc); ^{1}H NMR (CDCl$_3$, 270 MHz,
mixture of anomers) δ 6.33 (d, J = 2.0 Hz, 1H, H-1α),
5.67 (d, J = 8.2 Hz, 1H, H-1β), 5.26-5.38 (m, 5H), 5.06
(dd, J = 10.4, 3.4 Hz, 1H, H-3b), 4.27 (q, J = 6.6 Hz,
1H, H-5α), 3.95 (q, J = 6.3 Hz, 1H, H-5β), 2.23 (s,
3H), 2.19 (s, 3H), 2.18 (s, 3H), 2.17 (s, 3H), 2.15 (s,

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3H), 2.04 (s, 3H), 2.02 (s, 3H), 2.01 (s, 3H), 1.22 (d,
J = 6.6 Hz, 3H, H-6β), 1.16 (d, J = 6.6 Hz, 3H, H-6α).

To a solution of L-fucose tetraacetate 1 (1.76 g,
5.30 mmol) in 50 mL of CH_2Cl_2 is added thiophenol (1.4
mL, 1.46 g, 13.2 mmol) followed by BF_3·OEt_2 (3.3 mL,
3.76 g, 26.5 mmol). The reaction mixture is stirred at
room temperature for 17 h and then quenched by the
addition of 5 mL of H_2O. The reaction mixture is
diluted with 200 mL of CH_2Cl_2, washed with H_2O (100 mL),
saturated NaCl (100 mL), dried over Na_2SO_4, filtered
and concentrated to afford 2.77 g of a clear oil, which
is purified by flash chromatography (17%
EtOAc/petroleum ether) to give 1.36 g (67%) of phenyl
6-deoxy-2,3,4-tri-O-acetyl-1-thio-L-galactopyranoside 2
as a 3.5:1 (β:α) mixture of anomers. The anomers could
be separated by flash chromatography (17%
EtOAc/petroleum ether): R_f (β-anomer) 0.19 (17%
EtOAc/petroleum ether); R_f (α-anomer) 0.26 (17%
EtOAc/petroleum ether); ^{1}H NMR ($CDCl_3$, 300 MHz) β-
anomer, δ 7.41-7.55 (m, 2H), 7.22-7.37 (m, 3H), 5.20-
5.30 (m, 2H), 5.05 (dd, J = 9.9, 3.3 Hz, 1H, H-3), 4.70
(d, J = 9.9 Hz, 1H, H-1), 3.84 (q, J = 6.4 Hz, 1H, H-
5), 2.15 (s, 3H), 2.09 (s, 3H), 1.98 (s, 3H), 1.24 (d,
J = 6.6 Hz, 3H, H-6); α-anomer, δ 7.48-7.53 (m, 2H),
7.16-7.45 (m, 3H), 5.93 (d, J = 5.1 Hz, 1H, H-1), 5.27-
5.41 (m, 3H), 4.61 (q, J = 6.6 Hz, 1H, H-5), 2.17 (s,
3H), 2.11 (s, 3H), 2.02 (s, 3H), 1.13 (d, J = 6.6 Hz,
3H, H-6).

To a solution of phenyl 6-deoxy-2,3,4-tri-O-
acetyl-1-thio-β-L-galactopyranoside 2 (0.892 g, 2.33
mmol) in 25 mL of methanol is added K_2CO_3 (0.644 g,
4.66 mmol). The reaction mixture is stirred at room
temperature for 12 h. Amberlite resin (H· form) is
added to the reaction mixture and stirred for an
additional 30 min. The neutralized mixture is then
filtered through Celite, which is washed several times

with methanol, and the filtrate is concentrated to
afford 1.39 g of phenyl 6-deoxy-1-thio-β-L-
galactopyranoside 3 as a yellow oil, which is used in
the next step without further purification. The
thioglycoside 3 can be purified using flash
chromatography (10% MeOH/CH₂Cl₂): R_f 0.28 (10%
MeOH/CH₂Cl₂); ^{1}H NMR (C₆D₆, 270 MHz) δ 7.54-7.58 (m, 2H),
7.28-7.37 (m, 3H), 4.50 (d, J = 8.2 Hz, 1H, H-1), 3.70
(q, J = 6.6 Hz, 1H, H-5), 3.56-3.75 (m, 3H), 1.38 (d, J
= 6.6 Hz, 3H).

To a solution of crude phenyl 6-deoxy-1-thio-β-L-
galactopyranoside 3 in 15 mL of pyridine is added
pivaloyl chloride (4.0 mL, 3.90 g, 32.5 mmol) and DMAP
(0.33 g, 2.71 mmol). The reaction mixture is heated at
100 °C for 12 h, cooled, diluted with 50 mL of CH₂Cl₂,
washed with H₂O (100 mL) and saturated NaCl (100 mL),
dried over Na₂SO₄, filtered and concentrated to afford
3.25 g of phenyl 6-deoxy-2,3,4-tri-O-pivaloyl-1-thio-β-
L-galactopyranoside 4 as a brown oil. This oil is
purified by flash chromatography (15% EtOAc/petroleum
ether) to afford 0.53 g (48%) of the pure compound. An
additional 0.81 g of a brown oil, which that appeared
to be a mixture of incompletely acylated products, is
also isolated. This material is resubjected to the
reaction conditions for 48 h and provided an additional
0.21 g (19%, total yield 67% for 2 steps): R_f 0.48 (15%
EtOAc/petroleum ether); ^{1}H NMR (CDCl₃, 270 MHz) δ 7.50-
7.59 (m, 2H), 7.23-7.35 (m, 3H), 5.16-5.30 (m, 2H),
5.08 (dd, J = 9.9, 3.0 Hz, 1H, H-3), 4.66 (d, J = 9.6
Hz, 1H, H-1), 3.90 (q, J = 6.3 Hz, 1H, H-5), 1.21 (s,
9H), 1.18 (s, 9H), 1.21 (s, 9H), 1.21 (d, J = 6.6 Hz,
3H, H-6); ^{13}C NMR (CDCl₃, 68 MHz) δ 177.2, 177.4, 177.1,
133.5, 131.1, 128.6, 128.4, 128.1, 127.7, 85.1, 73.3,
72.6, 69.9, 66.3, 38.9, 38.6, 26.9, 27.0, 16.4; FABMS
C₂₇H₃₉O₇S (MNa⁻) calcd 531.2392, found 531.2404.

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To a solution of phenyl 6-deoxy-2,3,4-tri-*O*-pivaloyl-1-thio-β-L-galactopyranoside 4 (2.47 g, 5.22 mmol) in 65 mL of CH_2Cl_2 at -78 °C is added mCPBA (1.53 g, 8.84 mmol). The reaction mixture is allowed to warm to -15 °C and then quenched with methyl sulfide (5.3 mL, 4.48 g, 17.4 mmol) and allowed to warm to room temperature. The reaction mixture is then diluted with 50 mL CH_2Cl_2, extracted with H_2O (100 mL), saturated $NaHCO_3$ (100 mL), saturated NaCl (100 mL), dried over Na_2SO_4, filtered and concentrated to afford a white solid. The sulfoxide is purified using flash chromatography (15% EtOAc/petroleum ether) to afford 1.81 g (66%) of 1,6-dideoxy-2,3,4-tri-*O*-pivaloyl-1-(phenylsulfinyl)-β-L-galactopyranose 5 as a mixture of diastereomers: R_f 0.05 and 0.13 (15% EtOAc/petroleum ether).

7.2.   1,6-Dideoxy-1-(phenylsulfinyl)-2,3,4-tri-*O*-pivaloyl-β-D-galactopyranose (β-D-5)

By the above method, but beginning with D-fucose, the title compound is prepared.

7.3.   3-Azido-4-*O*-benzoyl-1,3,6-trideoxy-2-*O*-pivaloyl-1-(phenylsulfinyl)-β-L-galactopyranose (20)

To a solution of L-fucose phenylthioglycoside (phenyl 6-deoxy-1-thio-L-galactopyranoside, 3, prepared above) (3.4 g, 13 mmol) in 250 mL of DMF is added p-toluenesulfonic acid hydrate (1.3 g, 6.6 mmol) and 2,2-dimethoxypropane (3.3 mL, 27 mmol). The reaction mixture is stirred at room temperature for 12 h and then quenched by the addition of 10 mL of saturated $NaHCO_3$. The reaction mixture is diluted with 400 mL of CH_2Cl_2, washed with saturated $NaHCO_3$ (2 x 200 mL), dried over Na_2SO_4, filtered, concentrated and purified by flash chromatography (8%

EtOAc/petroleum ether) to give 3.3 g (85%) of phenyl 6-
deoxy-3,4-O-isopropylidene-1-thio-L-galactopyranoside 6
as a mixture of anomers. The anomers could be
separated by flash chromatography: R$_f$ (α-6) 0.58 (50%
EtOAc/petroleum ether); R$_f$ (β-anomer) 0.46 (50%
EtOAc/petroleum ether); ^{1}H NMR of β-6 (CDCl$_3$, 300 MHz)
δ 7.70-7.55 (m, 2H, ArH), 7.45-7.28 (m, 3H, ArH), 4.48
(d, J = 10 Hz, 1H, H-1), 4.15-4.10 (m, 2H, H-3 and H-
4), 3.96 (q, J = 4.8 Hz, 1H, H-5), 3.62 (q, J = 4.0 Hz,
1H, H-2), 2.52 (s, br, 1H, OH), 1.53-1.50 (m, 6H, H-6
and CH$_3$), 1.42 (s, 3H, CH$_3$).

To a solution of phenyl 6-deoxy-3,4-O-
isopropylidene-1-thio-L-galactopyranoside 6 mixed
anomers (2.12 g, 7.16 mmol) in 140 mL of DMF is added
NaH (568 mg, 14.2 mmol), and the reaction mixture
stirred for 10 min. p-Methoxybenzyl chloride (1.9 mL,
14.2 mmol) is added, and the solution is stirred for 30
min and then quenched with 10 mL of saturated NaHCO$_3$.
The reaction mixture is diluted with 300 mL of CH$_2$Cl$_2$,
washed with saturated NaHCO$_3$ (150 mL), dried over
Na$_2$SO$_4$, filtered and concentrated. The crude product
is purified by flash chromatography (8% EtOAc/petroleum
ether) to give 2.6 g (87%) of phenyl 6-deoxy-3,4-O-
isopropylidene-2-(4-methoxybenzyl)-1-thio-L-
galactopyranoside 7 as a mixture of anomers: R$_f$ 0.50
(35% EtOAc/petroleum ether); ^{1}H NMR of β-7 (CDCl$_3$, 300
MHz) δ 7.60 (d, 2H, ArH), 7.43-7.28 (m, 5H, ArH), 6.94
(d, 2H, ArH), 4.82 (d, J = 10.6 Hz, 1H, CH$_2$), 4.67 (d,
J = 10.6 Hz, 1H, CH$_2$), 4.65 (d, J = 9.9 Hz, 1H, H-1),
4.29 (t, J = 5.9 Hz, 1H, H-2), 4.13 (dd, J = 5.9, 2.2
Hz, 1H, H-3), 3.91-3.86 (m, 4H, H-4, OCH$_3$), 3.56 (dd, J
= 6.2, 3.3 Hz, 1H, H-5), 1.50 (s, 3H, CH$_3$), 1.47 (d, J
= 6.2 Hz, 3H, H-6) 1.44 (s, 3H, CH$_3$).

To a solution of phenyl 6-deoxy-3,4-O-
isopropylidene-2-(4-methoxybenzyl)-1-thio-L-
galactopyranoside 7 mixed anomers (2.4 g, 5.8 mmol) in

60 mL of MeOH is added TsOH•H₂O (540 mg, 2.9 mmol).
The reaction mixture is stirred at room temperature for
5 h and then neutralized with Amberlite resin (OH⁻
form). The solution is filtered, washed several times
with MeOH and then concentrated *in vacuo*. The product
is purified by flash chromatography (60%
EtOAc/petroleum ether) to give 2.06 g (95%) of isolated
anomers of phenyl 6-deoxy-2-(4-methoxybenzyl)-1-thio-L-
galactopyranoside 9. ^{1}H NMR (CDCl₃, 300 MHz) of β-9:
δ 7.65 (d, 2H, ArH), 7.40-7.37 (m, 5H, ArH), 6.96 (d,
2H, ArH), 4.95 (d, J = 10.6 Hz, 1H, CH₂), 4.69 (d, J =
10.6 Hz, 1H, CH₂), 4.67 (d, J = 9.5 Hz, 1H, H-1), 3.87
(s, 3H, OCH₃), 3.79 (d, J = 2.9 Hz, 1H, H-4), 3.72-3.58
(m, 3H, H-2, H-3, H-5), 2.46 (s, br, 2H, OH), 1.42 (d,
J = 6.2 Hz, 3H, H-6); α-9, δ 7.56 (d, 2H, ArH), 7.43-
7.31 (m, 5H, ArH), 6.95 (d, 2H, ArH), 5.78 (d, J = 5.7
Hz, 1H, H-1), 4.78 (d, J = 11.5 Hz, 1H, CH₂), 4.58 (d,
J = 11.5 Hz, 1H, CH₂), 4.50 (q, J = 6.4 Hz, 1H, H-5),
4.12 (dd, J = 5.7, 9.6 Hz, 1H, H-3), 3.97-3.82 (m, 5H,
H-2, H-4, OCH₃), 3.18 (s, br, 1H, OH), 2.88 (s, br, 1H,
OH), 1.40 (d, J = 6.4 Hz, 3H, H-6).

Trifluoromethanesulfonic anhydride (2.5 mL, 15
mmol) is added dropwise to a cooled (0 °C) solution of
phenyl 6-deoxy-2-(4-methoxybenzyl)-1-thio-β-L-
galactopyranoside (β-9) (1.4 g, 3.8 mmol) and pyridine
(3.0 mL, 38 mmol) in 50 mL of CH₂Cl₂. The solution is
stirred at 0 °C for 45 min and is allowed to warm to
room temperature over 3 h. The reaction mixture is
then cooled to 0 °C before quenching with TEA (1 mL,
7.2 mmol). The reaction mixture is diluted with 25 mL
of CH₂Cl₂, extracted with saturated NaHCO₃ (2 x 50 mL),
dried over Na₂SO₄, filtered, concentrated and purified
by flash chromatography (8% EtOAc/petroleum ether) to
give phenyl 6-deoxy-3,4-di-*O*-trifluoromethanesulfonyl-
2-(4-methoxybenzyl)-1-thio-β-L-galactopyranoside (β-
12): R_f 0.44 (20% EtOAc/petroleum ether); ^{1}H NMR (CDCl₃,

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270 MHz) δ 7.60-7.57 (m, 2H, ArH), 7.38-7.33 (m, 5H, ArH), 6.90 (d, 2H, ArH), 5.16 (d, J = 2.3 Hz, 1H, H-4), 4.92 (dd, J = 2.3, 9.6 Hz, 1H, H-3), 4.80 (d, J = 9.2 Hz, 1H, CH$_2$), 4.65 (d, J = 9.6 Hz, 1H, H-1), 4.63 (d, J = 9.2 Hz, 1H, CH$_2$), 3.83-3.76 (m, 5H, H-2, H-5, OCH$_3$), 1.45 (d, J = 6.6 Hz, 3H, H-6).

To a solution of the above bis(triflate) β-12 in 40 mL of toluene is added potassium benzoate (1.8 g, 11 mmol) and 18-crown-6 (3.0 g, 11 mmol). The reaction mixture is stirred at room temperature for 5 h and then diluted with 40 mL of CH$_2$Cl$_2$. The resulting solution is washed with saturated NaHCO$_3$ (2 x 50 mL), dried over Na$_2$SO$_4$, filtered and concentrated. The crude phenyl 6-deoxy-3,4-di-O-benzoyl-2-O-(4-methoxybenzyl)-1-thio-β-L-allopyranoside (β-13) is used without further purification in the next step. However, the material can be purified by flash chromatography (10% EtOAC/petroleum ether): R$_f$ 0.59 (20% EtOAc/petroleum ether); ^{1}H NMR (CDCl$_3$, 270 MHz) δ 8.02 (d, 2H, ArH), 7.85 (d, 2H, ArH), 7.61-7.23 (m, 9H, ArH) 6.83 (d, 2H, ArH), 6.16 (t, J = 3.0 Hz, 1H, H-3), 5.17 (d, J = 9.6 Hz, 1H, H-1), 4.95 (dd, J = 2.6, 9.9 Hz, 1H, H-4), 4.66 (d, J = 10.9 Hz, 1H, CH$_2$), 4.37 (d, J = 10.9 Hz, 1H, CH$_2$), 4.24 (dq, J = 6.3, 9.9 Hz, 1H, H-5), 3.78 (s, 3H, OCH$_3$), 3.60 (dd, J = 3.0, 9.6 Hz, 1H, H-2), 1.33 (d, J = 6.3 Hz, 3H, H-6).

To a solution of crude phenyl 6-deoxy-3,4-di-O-benzoyl-2-O-(4-methoxybenzyl)-1-thio-β-L-allopyranoside β-13 in 20 mL of MeOH is added NaOMe (200 mg, 3.8 mmol). The reaction mixture is stirred at room temperature for 2 h and then neutralized with Amberlite resin. The solution is filtered, washed several times with MeOH and concentrated in vacuo. The crude product is purified by flash chromatography (60% EtOAc/petroleum ether) to afford 1.01 g (72%, 3 steps) of phenyl 6-deoxy-2-O-(4-methoxybenzyl)-1-thio-β-L-

allopyranoside .(β-14): R. 0.35 (50% EtOAc/petroleum
ether); 'H NMR (CDCl₃, 270 MHz) δ 7.56-7.52 (m, 2H,
ArH), 7.31-7.27 (m, 5H, ArH), 6.89-6.88 (m, 2H, ArH),
4.93 (d, J = 9.9 Hz, 1H, H-1), 4.71 (d, J = 11.2 Hz,
1H, CH₂), 4.55 (d, J = 11.2 Hz, 1H, CH₂), 4.13 (t, J =
2.6 Hz, 1H, H-3), 3.83 (s, 3H, OCH₃), 3.73-3.63 (m, 1H,
H-5), 3.38 (dd, J = 3.3, 9.9 Hz, 1H, H-2), 3.21 (dt, J
= 3.3, 9.6 Hz, 1H, H-4), 2.58 (s, 1H, OH) 2.34-2.30 (d,
1H, OH), 1.33 (d, J = 6.3 Hz, 3H, H-6).

    Trifluoromethanesulfonic anhydride (1.8 mL, 10.8
mmol) is added at 0 °C to a solution of phenyl 6-deoxy-
2-O-(4-methoxybenzyl)-1-thio-β-L-allopyranoside (β-14)
(1.01 g, 2.69 mmol) and pyridine (2.2 mL, 26.9 mmol) in
30 mL of CH₂Cl₂. The solution is stirred at 0 °C for 1
h and allowed to warm at room temperature over 3 h.
The reaction mixture is cooled to 0 °C before quenching
with TEA (1.0 mL, 7.2 mmol). The reaction mixture is
diluted with 30 mL of CH₂Cl₂, washed with saturated
NaHCO₃ (30 mL), 1N HCl (30 mL), dried over Na₂SO₄,
filtered and concentrated. The crude product is
purified by flash chromatography (8% EtOAc/petroleum
ether) to give 1.36 g (79%) of phenyl 6-deoxy-3,4-di-O-
(trifluoromethanesulfonyl)-2-O-(4-methoxybenzyl)-1-
thio-β-L-allopyranoside (β-15): R. 0.49 (20%
EtOAc/petroleum ether); 'H NMR (CDCl₃, 270 MHz) δ 7.48
(d, 2H, ArH), 7.33-7.21 (m, 5H, ArH), 6.91 (d, 2H,
ArH), 5.34 (t, J = 2.0 Hz, 1H, H-3), 4.93 (d, J = 9.2
Hz, 1H, H-1), 4.77 (d, J = 11.2 Hz, 1H, CH₂), 4.65 (d,
J = 11.2 Hz, 1H, CH₂), 4.55 (dd, J = 2.0, 8.8 Hz, 1H,
H-4), 4.19-3.96 (m, 1H, H-5), 3.90 (s, 3H, OCH₃), 3.47
(dd, J = 2.0, 9.2 Hz, 1H, H-2), 1.36 (d, J = 5.8 Hz,
3H, H-6).

    The above bis(triflate) β-15 (297 mg, 2.13 mmol)
is dissolved in 10 mL of DMF and cooled at -15 °C. To
the solution is added NaN₃ (137 mg, 2.11 mmol) and the
reaction mixture is stirred at -15 °C for 45 minutes.

Potassium benzoate (511 mg, 3.20 mmol) and 18-crown-6
(844 mg, 3.20 mmol) are added to the reaction mixture.
The reaction mixture is stirred for 8 h and is then
diluted with 20 mL of CH_2Cl_2. The resulting solution
is washed with $NaHCO_3$ (3 x 20 mL), dried over Na_2SO_4,
filtered and concentrated. The resulting phenyl 3-
azido-4-O-benzoyl-3,6-di-deoxy-2-O-(4-methoxybenzyl)-1-
thio-β-L-galactopyranoside (β-16) is purified by flash
chromatography (20% EtOAc/petroleum ether) and taken on
immediately to the next step: R_f 0.35 (20%
EtOAc/petroleum ether); ^1H NMR ($CDCl_3$, 270 MHz) δ 8.01
(d, 2H, ArH), 7.71-7.26 (m, 10H, ArH), 6.90 (d, 2H,
ArH), 5.47 (d, J = 2.0 Hz, 1H, H-4), 4.91 (d, J = 9.6
Hz, 1H, CH_2), 4.69 (d, J = 9.2 Hz, 1H, H-1), 4.64 (d, J
= 9.6 Hz, 1H, CH_2), 3.85-3.64 (m, 6H, H-2, H-3, H-5,
OCH_3), 1.27 (d, J = 6.3 Hz, 3H, H-6).

To a solution of phenyl 3-azido-4-O-benzoyl-3,6-
di-deoxy-2-O-(4-methoxybenzyl)-1-thio-β-L-
galactopyranoside (β-16) in 50 mL of CH_2Cl_2 is added 5
mL of TFA (10% TFA/CH_2Cl_2). The reaction mixture is
immediately diluted with 150 mL of CH_2Cl_2 and
neutralized with $NaHCO_3$ (20 mL). The resulting
suspension is washed with $NaHCO_3$ (100 mL), dried over
Na_2SO_4, filtered and concentrated. The crude product
is purified by flash chromatography (20%
EtOAc/petroleum ether) to give 541 mg (66%, 2 steps) of
phenyl 3-azido-4-O-benzoyl-3,6-di-deoxy-1-thio-β-L-
galactopyranoside (β-18): R_f 0.21 (30% EtOAc/petroleum
ether); ^1H NMR ($CDCl_3$, 270 MHz) δ 7.88-7.85 (m, 2H,
ArH), 7.68-7.56 (m, 3H, ArH), 7.47-7.35 (m, 5H, ArH),
5.44 (d, J = 2.3 Hz, 1H, H-4), 4.57 (d, J = 8.9 Hz, 1H,
H-1), 3.92 (q, J = 6.3 Hz, 1H, H-5), 3.83 (dd, J = 2.3,
9.9 Hz, 1H, H-3), 3.74 (dt, J = 2.0, 9.9 Hz, 1H, H-2),
2.62 (d, J = 2.0, 1H, OH), 1.26 (d, J = 6.3 Hz, 3H, H-
6).

To a solution of phenyl 3-azido-4-O-benzoyl-3,6-
di-deoxy-1-thio-β-L-galactopyranoside (β-18) (118 mg,
0.307 mmol) in 5 mL of CH₂Cl₂ is added TEA (256 μL, 1.87
mmol), pivaloyl chloride (114 μL, 0.921 mmol) and DMAP
(19 mg, 0.154 mmol). The reaction mixture is stirred
at room temperature for 12 h, diluted with 15 mL of
CH₂Cl₂, washed with 1M HCl (2 x 10 mL), dried over
Na₂SO₄, filtered and concentrated. The crude product
is purified by flash chromatography (20%
EtOAc/petroleum ether) to give 114 mg (80%) of phenyl
3-azido-4-O-benzoyl-3,6-di-deoxy-2-O-pivaloyl-1-thio-β-
L-galactopyranoside (β-19): R$_f$ 0.54 (20%
EtOAc/petroleum ether); ¹H NMR (CDCl₃, 270 MHz) δ 7.93
(d, 2H, ArH), 7.59-7.56 (m, 3H, ArH), 7.46-7.26 (m, 5H,
ArH), 5.53 (d, J = 2.6 Hz, 1H, H-4), 5.25 (t, J = 9.9
Hz, 1H, H-2) 4.73 (d, J = 9.9 Hz, 1H, H-1), 3.92 (q, J
= 6.3 Hz, 1H, H-5), 3.79 (dd, J = 2.6, 9.9 Hz, 1H, H-
3), 1.42-1.21 (m, 12H, H-6, CH₃); ¹³C NMR (CDCl₃, 68
MHz) δ 176.8, 165.9, 133.8, 133.7, 131.8, 130.2, 129.0,
128.9, 128.6, 128.4, 86.1, 74.4, 71.6, 68.3, 63.9,
39.1, 27.3, 16.9; FABMS C₂₄H₂₇O₅N₃ (MNa⁺) calcd 492.1569,
found 492.1579.

To a solution of phenyl 3-azido-4-O-benzoyl-3,6-
di-deoxy-2-O-pivaloyl-1-thio-β-L-galactopyranoside (β-
19) (270 mg, 0.575 mmol) in 10 mL of CH₂Cl₂ at -78 °C is
added a solution of mCPBA (159 mg of 64% material,
0.920 mmol) in 2 mL of CH₂Cl₂. The reaction mixture is
allowed to warm to -20 °C and then quenched with TEA
(500 μL, 3.59 mmol). The reaction mixture is diluted
with 10 mL of CH₂Cl₂, washed with saturated NaHSO₃ (10
mL), saturated NaHCO₃ (10 mL), dried over Na₂SO₄,
filtered and concentrated. The crude product is
purified by flash chromatography (60% EtOAc/petroleum
ether) to give 231 mg (83%) of 3-azido-4-O-benzoyl-
1,3,6-tri-deoxy-2-O-pivaloyl-1-(phenylsulfinyl)-β-L-

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galactopyranose (β-20) as a mixture of diastereomers:
R_f 0.26 (50% EtOAc/petroleum ether).

    7.4.   3-Azido-4-O-benzoyl-1,3,6-trideoxy-2-O-
                pivaloyl-1-(phenylsulfinyl)-β-D-
                galactopyranose (β-D-20)

        By the method above, but beginning with D-
fucose, the title compound is prepared.

    7.5.   1,6-Dideoxy-2-(4-methoxybenzyl)-1-
                (phenylsulfinyl)-α-L-galactopyranose 3,4-
                carbonate (α-11)

        To a solution of phenyl 6-deoxy-2-(4-
methoxybenzyl)-1-thio-α-L-galacto-pyranoside (α-9,
prepared above) (743 mg, 1.98 mmol) in 40 mL of THF is
added 1,1'-carbonyldiimidazole (422 mg, 2.60 mmol).
The reaction mixture is stirred at room temperature for
24 h and then quenched with 5 mL of 1M HCl. The
resulting suspension is diluted with 40 mL of CH₂Cl₂,
washed with of 1M HCl (15 mL), dried over Na₂SO₄,
filtered and concentrated. The crude product is
purified by flash chromatography (35% EtOAc/petroleum
ether) to give 766 mg (97%) of phenyl 6-deoxy-2-(4-
methoxybenzyl)-1-thio-α-L-galactopyranoside 3,4-
carbonate (α-10): R_f 0.40 (40% EtOAc/petroleum ether);
^{1}H NMR (CDCl₃, 300 MHz) δ 7.50 (d, 2H, ArH), 7.38-7.32
(m, 5H, ArH), 6.96 (d, 2H, ArH), 5.74 (d, J = 5.6 Hz,
1H, H-1), 4.81 (d, J = 11.2 Hz, 1H, CH₂), 4.74 (dd, J =
5.1, 9.6 Hz, 1H, H-3), 4.67-4.60 (m, 2H, H-4 and CH₂),
4.53 (q, J = 6.1, 1H, H-5), 4.23-4.18 (m, 1H, H-2),
3.88 (s, 3H, CH₃), 1.35 (d, J = 6.1 Hz,3H, H-6); ^{13}C NMR
(CDCl₃, 68 MHz) δ 160.0, 154.0, 134.4, 131.7, 130.0,
129.1, 128.8, 127.6, 114.2, 86.5, 76.5, 74.7, 73.5,
72.7, 65.0, 55.5, 15.6.

        To a solution of phenyl 6-deoxy-2-(4-
methoxybenzyl)-1-thio-α-L-galactopyranoside 3,4-
carbonate (α-10) (280 mg, 0.691 mmol) in 10 mL of

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CH₂Cl₂ at -78 °C is added a solution of mCPBA (173 mg, 1.11 mmol) in 2 mL of CH₂Cl₂. The reaction mixture is allowed to warm to -20 °C and then quenched with TEA (500 μL, 3.59 mmol). The reaction mixture is diluted with 10 mL of CH₂Cl₂, washed with saturated NaHSO₃ (10 mL), saturated NaHCO₃ (10 mL), dried over Na₂SO₄, filtered and concentrated. The crude product is purified by flash chromatography (60% EtOAc/petroleum ether) to give 266 mg (92%) of 1,6-dideoxy-2-(4-methoxybenzyl)-1-(phenylsulfinyl)-α-L-galactopyranose 3,4-carbonate (α-11) as a mixture of diastereomers: R₁ 0.26 (50% EtOAc/petroleum ether).

7.6. 1,6-Dideoxy-2-(4-methoxybenzyl)-1-(phenylsulfinyl)-α-D-galactopyranose 3,4-carbonate (α-D-11)

By the method above, but beginning with D-fucose, the title compound is prepared.

7.7. 1,6-Dideoxy-3,4-O-isopropylidene-2-(4-methoxybenzyl)-1-(phenylsulfinyl)-β-L-galactopyranose (8)

To a solution of phenyl 6-deoxy-3,4-O-isopropylidene-2-(4-methoxybenzyl)-1-thio-L-galactopyranoside (7, prepared above), (290 mg, 0.69 mmol) in 10 mL of CH₂Cl₂ at -78 °C is added a solution of mCPBA (170 mg, 1.1 mmol) in 2 mL of CH₂Cl₂. The reaction mixture is allowed to warm to -20 °C and then quenched with TEA (500 μL, 3.59 mmol). The reaction mixture is diluted with 10 mL of CH₂Cl₂, washed with saturated NaHSO₃ (10 mL), saturated NaHCO₃ (10 mL), dried over Na₂SO₄, filtered and concentrated. The crude product is purified by flash chromatography (EtOAc/petroleum ether) to give 1,6-dideoxy-3,4-O-isopropylidene-2-(4-methoxybenzyl)-1-(phenylsulfinyl)-L-galactopyranose (8) as a mixture of diastereomers.

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7.8.   1,6-Dideoxy-3,4-O-isopropylidene-2-(4-
        methoxybenzyl)-1-(phenylsulfinyl)-D-
        galactopyranose (D-8)

        By the method above, but beginning with D-
fucose, the title compound is prepared.

7.9.   3,4-Di-O-benzoyl-1,6-dideoxy-2-O-(4-
        methoxybenzyl)-1-(phenylsulfinyl)-β-L-
        allopyranose (β-13 sulfoxide)

        To a solution of phenyl 6-deoxy-3,4-di-O-
benzoyl-2-O-(4-methoxybenzyl)-1-thio-β-L-allopyranoside
(β-13, prepared above) (400 mg, 0.7 mmol) in 10 mL of
CH₂Cl₂ at -78 °C is added a solution of mCPBA (170 mg,
1.1 mmol) in 2 mL of CH₂Cl₂. The reaction mixture is
allowed to warm to -20 °C and then quenched with TEA
(500 µL, 3.59 mmol). The reaction mixture is diluted
with 10 mL of CH₂Cl₂, washed with saturated NaHSO₃ (10
mL), saturated NaHCO₃ (10 mL), dried over Na₂SO₄,
filtered and concentrated. The crude product is
purified by flash chromatography (EtOAc/petroleum
ether) to give 1,6-dideoxy-3,4-di-O-benzoyl-2-O-(4-
methoxybenzyl)-1-(phenylsulfinyl)-β-L-allopyranose as a
mixture of diastereomers.

7.10.   3,4-Di-O-benzoyl-1,6-dideoxy-2-O-(4-
        methoxybenzyl)-1-(phenylsulfinyl)-β-D-
        allopyranose (β-D-13 sulfoxide)

        By the method above, but beginning with D-
fucose, the title compound is prepared.

7.11.   3-Azido-4-O-benzoyl-1,3,6-trideoxy-2-O-(4-
        methoxybenzyl)-1-(phenylsulfinyl)-β-L-
        galactopyranose (β-17)

        To a solution of phenyl 3-azido-4-O-
benzoyl-3,6-di-deoxy-2-O-(4-methoxybenzyl)-1-thio-β-L-
galactopyranoside (β-16, prepared above), (350 mg, 0.7
mmol) in 10 mL of CH₂Cl₂ at -78 °C is added a solution
of mCPBA (170 mg, 1.1 mmol) in 2 mL of CH₂Cl₂. The

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reaction mixture is allowed to warm to -20 °C and then
quenched with TEA (500 μL, 3.59 mmol). The reaction
mixture is diluted with 10 mL of CH_2Cl_2, washed with
saturated $NaHSO_3$ (10 mL), saturated $NaHCO_3$ (10 mL),
dried over Na_2SO_4, filtered and concentrated. The
crude product is purified by flash chromatography
(EtOAc/petroleum ether) to give the title compound as a
mixture of diastereomers.

7.12. 3-Azido-4-O-benzoyl-1,3,6-trideoxy-2-O-(4-methoxybenzyl)-1-(phenylsulfinyl)-β-D-galactopyranose (β-D-17)

By the method above, but beginning with D-
fucose, the title compound is prepared.

7.13. 2-Azido-1,2,6-trideoxy-1-(phenylsulfinyl)-α-L-galactopyranose 3,4-carbonate (α-25)

The mixed anomers of 1,3,4-tri-O-acetyl-2-
azido-2,6-dideoxy-L-galactopyranoside (21) are prepared
from L-fucose by the method of A. Anisuzzaman and D.
Horton, *Carb. Res.*, **169**, 258-262 (1987). To a solution
of 21 (3.80 g, 12.1 mmol) in 120 mL of CH_2Cl_2,
thiophenol (3.1 mL, 3.3 g, 30.1 mmol) and $BF_3 \bullet Et_2O$ (7.4
mL, 8.5 g, 60.3 mmol) are added at room temperature.
The reaction mixture is heated at 40 °C for 50 min,
then quenched with H_2O (20 mL). The organic layer is
washed with brine (100 mL), dried over Na_2SO_4, filtered
and concentrated to afford a mixture of anomers of
phenyl 2-azido-3,4-di-O-acetyl-2,6-dideoxy-1-thio-L-
galactopyranoside (22) as a clear oil: R_f 0.39 (25%
EtOAc/petroleum ether).

To a solution of 22 (4.40 g, 12.1 mmol) in 120 mL
of methanol is added K_2CO_3 (5.97 g, 36.2 mmol). The
reaction mixture is stirred at room temperature for 1.5
h and then neutralized with amberlite resin, filtered,
concentrated and purified by flash chromatography (5%
methanol/CH_2Cl_2) to yield 3.10 g (91%, 2 steps) of

phenyl 2-azido-2,6-dideoxy-1-thio-L-galactopyranoside
(23) as a 2.5:1 (α:β) mixture of anomers: R_f 0.10 (25%
EtOAc/petroleum ether); ^{1}H NMR (CDCl$_3$, 270 MHz) mixture
of anomers, δ 7.61-7.27 (m, 10H), 5.61 (d, J = 5.3 Hz,
1H, H-1α), 4.50 (q, J = 6.6 Hz, 1H, H-5α), 4.42 (d, J =
9.9 Hz, 1H, H-1β), 4.11 (dd, J = 10.1, 5.4 Hz, 2H, H-
3α,β), 3.88-3.85 (m, 3H), 3.73 (br s, 1H), 3.63 (q, J =
6.3 Hz, 1H, H-5β), 3.59-3.40 (m, 1H), 2.81 (br s, 1H,
OH), 2.47 (br s, 1H, OH), 2.23 (br s, 1H, OH), 1.72 (br
s, 1H, OH), 1.37 (d, J = 6.3 Hz, 3H, H-6β), 1.30 (d, J
= 6.6 Hz, 3H, H-6α).

To a solution of **23** (2.90 g, 10.3 mmol) in 100 mL
of CH$_2$Cl$_2$ at 0 °C is added 1,1'-carbonyldiimidazole
(3.34 g, 20.6 mmol). The reaction mixture is allowed
to warm to room temperature for 15 min and quenched
with 50 mL of H$_2$O. The aqueous layer is extracted with
CH$_2$Cl$_2$ (3 x 40 mL), and the organic layers are
combined, dried over Na$_2$SO$_4$, filtered, concentrated and
purified by flash chromatography (gradient elution with
15-25% EtOAc/petroleum ether) to yield 2.30 g (73%) of
phenyl 2-azido-2,6-dideoxy-1-thio-α-L-galactopyranoside
3,4-carbonate **24** as a white foam: R_f 0.38 (25%
EtOAc/petroleum ether). The β-anomer, R_f 0.22, is not
isolated. ^{1}H NMR (CDCl$_3$, 270 MHz) (α-**24**): δ 7.52-7.32
(m, 5H), 5.64 (d, J = 5.6 Hz, 1H, H-1), 4.90 (dd, J =
7.3, 5.6 Hz, 1H, H-3), 4.66 (dd, J = 7.6, 2.0 Hz, 1H,
H-4), 4.47 (dq, J = 6.6, 2.0 Hz, 1H, H-5), 4.30 (app t,
J = 5.6 Hz, 1H, H-2), 1.36 (d, J = 6.6 Hz, 3H, H-6);
^{13}C NMR (CDCl$_3$, 68 MHz) δ 153.5, 133.1, 132.0, 129.3,
128.2, 85.3, 76.3, 74.4, 64.5, 59.0, 15.7; FABMS
C$_{13}$H$_{13}$N$_3$O$_4$S (MNa$^+$) calcd 330.0524, found 330.0520.

To a solution of phenyl 2-azido-2,6-dideoxy-1-
thio-α-L-galactopyranoside 3,4-carbonate (α-**24**) (0.860
g, 2.80 mmol) in 50 mL of CH$_2$Cl$_2$ is added NaHCO$_3$ at room
temperature. The reaction mixture is then cooled to -
78 °C, and mCPBA (0.878 g, 2.80 mmol, 50-60%) is added.

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The reaction mixture is stirred at -78 °C for 30
minutes and then allowed to warm to -40 °C over 1 h.
The reaction is quenched with dimethyl sulfide (1 mL)
at -40 °C and then poured into a solution of saturated
NaHCO$_3$ (50 mL) and extracted with CH$_2$Cl$_2$ (3 x 30 mL).
The organic layers are combined, dried over Na$_2$SO$_4$,
filtered, concentrated and purified by flash
chromatography (40% EtOAc/petroleum ether) to afford
0.871 g (96%) of 2-azido-1,2,6-trideoxy-1-
(phenylsulfinyl)-α-L-galactopyranose 3,4-carbonate
(α-25) as a mixture of diastereomers: R$_f$ (major
diastereomer) 0.14 (40% EtOAc/petroleum ether).

> ### 7.14. 2-Azido-1,2,6-trideoxy-1-(phenylsulfinyl)-α-D-galactopyranose 3,4-carbonate (α-D-25)

By the method above, but beginning with D-
fucose, the title compound is prepared.

> ### 7.15. 2-Azido-3,4-di-O-acetyl-1,2,6-trideoxy-1-(phenylsulfinyl)-L-galactopyranose (26)

To a solution of phenyl 2-azido-3,4-di-O-
acetyl-2,6-dideoxy-1-thio-L-galactopyranoside (22)
(1.02 g, 2.80 mmol) in 50 mL of CH$_2$Cl$_2$ is added NaHCO$_3$
at room temperature. The reaction mixture is cooled to
-78 °C, and mCPBA (0.878 g, 2.80 mmol, 50-60%) is
added. The reaction mixture is stirred at -78 °C for
30 minutes and then allowed to warm to -40 °C over 1 h.
The reaction is quenched with dimethyl sulfide (1 mL)
at -40 °C and then poured into a solution of saturated
NaHCO$_3$ (50 mL) and extracted with CH$_2$Cl$_2$ (3 x 30 mL).
The organic layers are combined, dried over Na$_2$SO$_4$,
filtered, concentrated, and purified by flash
chromatography (EtOAc/petroleum ether) to afford the
title compound 26 as a mixture of diastereomers.

> ### 7.16. 2-Azido-3,4-di-O-acetyl-1,2,6-trideoxy-1-(phenylsulfinyl)-D-galactopyranose (D-26)

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By the method above, but beginning with D-fucose, the title compound is prepared.

7.17. 2,6-Bis-*O*-(4-methoxybenzyl)-1-deoxy-1-(phenylsulfinyl)-β-D-galactopyranose 3,4-carbonate (33)

By the method of A. Sarkar, K. Matta, *Carbohydr. Res.*, **233**, 245-250 (1992), 1,2,3,4,5,6-penta-*O*-acetyl-β-D-galactopyranose is converted into phenyl 1-thio-β-D-galactopyranoside (27).

To a solution of **27** (5.3 g, 20 mmol) in 100 mL of DMF is added 2,2-dimethoxypropane (6.0 mL, 49 mmol) and *p*-toluenesulfonic acid monohydrate (0.74 g, 3.9 mmol). The reaction is stirred at room temperature for 2 days and then diluted with water (150 mL) and extracted with CH_2Cl_2 (3 X 150 mL). The organic layers are combined, dried over Na_2SO_4 and concentrated *in vacuo*. The residue is purified by flash chromatography (100% EtOAc) to give 4.9 g (80%) of phenyl 3,4-*O*-isopropylidine-1-thio-β-D-galactopyranoside **28**, R_f 0.50 (100% EtOAc). ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.51-7.55 (m, 2H), 7.29-7.33 (m, 3H), 4.47 (d, *J* = 9.9 Hz, 1H, H-1), 4.18 (dd, *J* = 5.27, 1.65 Hz, 1H), 4.11 (appt, *J* = 6.3 Hz, 1H), 3.95-4.03 (m, 1H), 3.78-3.90 (m, 2H), 3.57 (dd, *J* = 10.2, 6.9 Hz, 1H), 1.41 (s, 3H), 1.33 (s, 3H).

To a solution of **28** (4.9 g, 16 mmol) in 120 mL of DMF at 0 °C is added NaH (1.5 g, 63 mmol). The solution is allowed to warm to room temperature over 0.5 h, and then *p*-methoxybenzyl chloride (8.5 mL, 63 mmol) and tetrabutylammonium iodide (4.1 g, 11 mmol) are added. After 4 h the reaction is quenched by pouring slowly into 500 mL of ice cold saturated $NaHCO_3$ with stirring. The product is extracted with CH_2Cl_2 (3 X 200 mL). The organic layers are dried over Na_2SO_4 and concentrated *in vacuo* to provide phenyl 2,6-bis-*O*-(4-methoxybenzyl)-3,4-*O*-isopropylidine-1-thio-β-D-galactopyranoside **29**, which is purified by flash

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chromatography (60% EtOAc/petroleum ether): R. 0.51; ¹H
NMR (CDCl₃, 270 MHz) δ 7.52-7.56 (m, 2H), 7.17-7.36 (m,
7H), 6.83-6.88 (m, 4H), 4.75 (d, J = 10.9 Hz, 1H),
4.42-4.69 (m, 4H), 4.18-4.26 (m, 2H), 3.88-3.93 (m,
1H), 3.75-3.80 (m, 8H), 3.49-3.57 (m, 1H), 1.42 (s,
3H), 1.35 (s, 3H).

The ketal **29** is dissolved in 100 mL of MeOH and *p*-
toluenesulfonic acid monohydrate (0.60 g, 3.1 mmol) is
added.   The reaction is stirred at room temperature
for 10 h and then saturated NaHCO₃ (50 mL) is added,
followed by water (100 mL).   The product is extracted
with CH₂Cl₂ (4 X 100 mL), and the organic layers are
combined, washed with saturated NaCl, (1 X 300 mL),
dried over Na₂SO₄ and concentrated *in vacuo*. The
residue is purified by flash chromatography (50%
EtOAc/petroleum ether) to give 5.4 g (68% over 2 steps)
of phenyl 2,6-bis-*O*-(4-methoxybenzyl)-1-thio-β-D-
galactopyranoside **31**: R_f 0.26 (50% EtOAc/petroleum
ether), ¹H NMR (CDCl₃, 270 MHz) δ 7.56-7.60 (m, 2H),
7.22-7.33 (m, 7H), 6.85-6.91 (m, 4H), 4.87 (d, J = 10.6
Hz, 1H, H-1), 4.58-4.65 (m, 2H), 4.50 (s, 2H), 4.02-
4.03 (m, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 3.75-3.77 (m,
2H), 3.59-3.62 (m, 3H).

To a solution **31** (5.4 g, 10 mmol) in 400 mL of
CH₂Cl₂ at 0 °C is added carbonyldiimidazole (2.5 g, 15
mmol). The solution is stirred at 0 °C for 20 min and
then for 12 h at room temperature. The solution is
then quenched by the addition of brine (100 mL). The
organic layer is dried over Na₂SO₄, and concentrated *in
vacuo*. The residue is purified by flash chromatography
(40% EtOAc/petroleum ether) to give 5.3 g (93%) of
phenyl 2,6-bis-*O*-(4-methoxybenzyl)-1-thio-β-D-
galactopyranoside 3,4-carbonate **32** as a syrup: R_f 0.69
(50% EtOAc/petroleum ether); ¹H NMR (CDCl₃, 270 MHz) δ
7.48-7.51 (m, 2H), 7.22-7.31 (m, 7H), 6.87-6.91 (m,
4H), 4.77-4.83 (m, 3H), 4.63 (s, 2H), 4.48 (s, 2H),

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3.96 (app t, J = 6.26 Hz, 1H), 3.82 (s, 6H), 3.67-3.75 (m, 3H); ^{13}C NMR (CDCl$_3$, 68 MHz) δ 159.8, 159.5, 153.9, 133.0, 132.2, 130.1, 129.9, 129.6, 129.2, 128.8, 128.1, 114.1, 114.0, 85.7, 78.1, 76.3, 74.8, 74.1, 73.6, 73.5, 68.0, 55.5.

To a solution of **32** (0.80 g 1.5 mmol) in 50 mL of CH$_2$Cl$_2$ at -78 °C is added 64% mCPBA (0.530 g, 1.96 mmol). The reaction is allowed to warm to -30 °C and quenched with dimethyl sulfide (0.3 mL, 4 mmol). Saturated NaHCO$_3$ (100 mL) is added and the product extracted with CH$_2$Cl$_2$ (2 X 150 mL). The organic layers are combined, dried over Na$_2$SO$_4$ and concentrated *in vacuo*. The residue is purified by flash chromatography (50% EtOAc/petroleum ether) to give 0.81 g (99%) of 2,6-bis-*O*-(4-methoxybenzyl)-1-deoxy-1-(phenylsulfinyl)-β-D-galactopyranose 3,4-carbonate **33** (a mixture of diastereomers) as a white foam: R$_f$ 0.19 (50% EtOAc/petroleum ether).

7.18.   2,6-Bis-*O*-(4-methoxybenzyl)-3,4-*O*-isopropylidine-1-deoxy-1-(phenylsulfinyl)-β-D-galactopyranose (30)

To a solution of **29** (1.5 mmol) in 50 mL of CH$_2$Cl$_2$ at -78 °C is added 64% mCPBA (0.530 g, 1.96 mmol). The reaction is allowed to warm to -30 °C and quenched with dimethyl sulfide (0.3 mL, 4 mmol). Saturated NaHCO$_3$ (100 mL) is added, and the product is extracted with CH$_2$Cl$_2$ (2 X 150 mL). The organic layers are combined, dried over Na$_2$SO$_4$ and concentrated *in vacuo*. The residue is purified by flash chromatography (EtOAc/petroleum ether) to give the title compound as a mixture of diastereomers.

7.19.   2,3,4,6-tetra-*O*-pivaloyl-1-deoxy-1-(phenylsulfinyl)-α-D-mannopyranose (37)

To a solution of D-mannose **34** (1.1 g, 6.1 mmol) in 30 mL of pyridine at room temperature is added

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pivaloyl chloride (4.5 mL, 36.6 mmol). The solution is
heated to 100°C for 48 hr and then allowed to cool.
The solvent is removed *in vacuo* and the residue is
dissolved in 50 mL of CH_2Cl_2 and washed with 5% HCl (4
x 60 mL), dried over Na_2SO_4, filtered, and concentrated
to afford a clear oil which is purified by flash
chromatography (10% EtOAc/hexane) to give 3.6 g (97%)
of penta(pivaloyl) D-mannose **35**, as a white solid, a
6:1 (α:β) mixture of anomers: R_f (β-anomer) 0.18 (10%
EtOAc/hexane); R_f (α-anomer) 0.1 (10% EtOAc/hexane); ^1H
NMR ($CDCl_3$, 300 MHz) δ 6.01 (d, J = 2.0Hz, 1H, H-1β),
5.83 (d, J = 1.0Hz, 1H, H-1α), 5.54-5.35 (m, 4H), 5.31-
5.27 (m, 1H), 5.16 (dd, J = 10.2, 3.0Hz, 1H, H-3α),
4.20-4.13 (m, 4H), 4.05-3.97 (m, 1H, H-5β), 3.87-3.81
(m, 1H, H-5α), 1.30 (s, 9H), 1.29 (s, 9H), 1.28 (s,
9H), 1.23 (s, 9H), 1.22 (s, 9H), 1.17 (s, 18H), 1.16
(s, 9H), 1.13 (s, 9H), 1.12 (s, 9H).

To a solution of **35** (3.6 g, 6.0 mmol) in 40 mL of
CH_2Cl_2 is added thiophenol (0.71 mL, 6.9 mmol) followed
by boron trifluoride diethyl ether complex (2.95 mL, 24
mmol). The reaction mixture is stirred at room
temperature for 10 hr and then quenched by the addition
of 20 ml of saturated $NaHCO_3$ solution. The reaction
mixture is then extracted with CH_2Cl_2 (3 x 30mL). The
combined organic layers are dried over Na_2SO_4,
concentrated, and purified by flash chromotography (8%
EtOAc/hexane) to give 3.1 g (85%) of phenyl 2,3,4,6-
tetra-O-pivaloyl-1-thio-α-D-mannopyranoside **36** as a
white solid: R_f 0.3 (8% EtOAc/hexane); ^1H NMR ($CDCl_3$,
300 MHz) δ 7.54-7.40 (m, 2H), 7.30-7.22 (m, 4H), 5.50
(m, 2H, H-4, H-2), 5.39 (d, J = 1.3Hz, 1H, H-1), 5.29
(dd, J = 10.2, 3.3Hz, 1H, H-3), 4.62 (m, 1H, H-5), 4.22
(dd, J = 12.5, 4.3Hz, 1H, H-6), 4.10 (dd, J = 12.5,
1.3Hz, 1H, H-6), 1.26 (s, 9H), 1.21 (s, 9H), 1.18 (s,
9H), 1.14 (s, 9H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 177.8,
176.9, 176.7, 176.4, 132.8, 131.8, 129.1, 127.9, 86.2,

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70.7, 69.9, 69.6, 65.0, 61.9, 38.7, 33.6, 32.5, 26.9,
26.4; FABMS $C_{32}H_{48}O_9S$ (MNa+) calcd 631. 2917, found
631.2943.

To a solution of 36 (1.38 g, 2.27 mmol) in 65 mL
of CH_2Cl_2 at -78 °C is added m-CPBA (612 mg, 64%, 2.27
mmol). The reaction mixture is allowed to warm to -15
°C and then quenched with dimethyl sulfide (1 mL, 13.6
mmol) and allowed to warm to room temperature. The
reaction mixture is diluted with 50 mL of CH_2Cl_2,
extracted with H_2O (100 mL), saturated $NaHCO_3$ (100 mL),
saturated NaCl (100 mL), dried over Na_2SO_4, filtered,
and concentrated to afford a white solid. The
sulfoxide is purified using flash chromatography (30%
EtOAc/hexane) to afford 1.07 g (76%) of the title
compound 37 as a mixture of diastereomers: R_f 0.35 and
0.38 (30% EtOAc/hexane).

7.20. 1-deoxy-1-(phenylsulfinyl)-2,3,4,6-tetra-O-pivaloyl-β-D-galactopyranose (41)

To a solution of galactose pentaacetate
(5.00 g, 12.8 mmol) in 125 mL of CH_2Cl_2 is added
thiophenol (1.49 mL, 14.1 mmol) and boron trifluoride
diethyl ether complex (4.73 mL, 38.4 mmol). The
reaction mixture is stirred at room temperature for 5 h
and then poured into 200 mL of ice water. The organic
layer is washed with saturated $NaHCO_3$ (200 ml), dried
over Na_2SO_4, filtered, concentrated and purified by
flash chromatography (35% EtOAc/hexane) to give 5.4 g
(96%) of 1-deoxy-1-(phenylthio)-2,3,4,6-tetra-O-acetyl-
β-D-galactopyranose 39: R_f 0.22 (35% EtOAc/hexane);
^{1}H NMR (CDCl$_3$, 270 MHz) δ 7.35-7.65 (m, 5 H, ArH),
5.50 (br d, J = 3.3 Hz, 1 H, H-4), 5.32 (t, J = 9.8 Hz,
1 H, H-2), 5.13 (dd, J = 9.8, 3.3 Hz, 1 H, H-3), 4.80
(d, J = 9.8 Hz, 1 H, H-1), 4.13-4.32 (m, 2 H, H-6, H-
6'), 4.02 (br t, J = 6.5 Hz, 1 H, H-5), 2.02-2.23 (4s,
12 H, OAc).

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To a solution of thioglycoside 39 (1.10 g, 2.5 mmol) in 50 mL of MeOH is added K₂CO₃ in small portions, until the reaction mixture tested basic to pH paper (pH 11). The reaction mixture is stirred at room temperature for 15 min and then neutralized with Amberlite resin (acid form). The resin is removed by filtration and washed with MeOH (2 x 50 mL). The filtrates are concentrated and azeotroped from toluene to remove the residue MeOH to afford 1-deoxy-1-(phenylthio)-β-D-galactopyranose which is taken on to the next step without further purification.

To a solution of 1-deoxy-1-(phenylthio)-β-D-galactopyranose (0.38 g, 1.4 mmol) in 25 mL of pyridine, pivaloyl chloride (1.75 mL, 14.0 mmol) and DMAP (0.200 g, 1.40 mmol) are added. The reaction mixture is stirred at 90-100 °C for 8 h. Pyridine is removed under reduced pressure, and the residue is dissolved in 100 mL of CH₂Cl₂ and washed with dilute HCl (100 mL), H₂O (100 mL), dried over Na₂SO₄, filtered, concentrated and purified by flash chromatography (10% EtOAc/hexane) to give 0.65 g (76%) of 1-deoxy-1-(phenylthio)-2,3,4,6-tetra-O-pivaloyl-β-D-galactopyranose **40**: R$_f$ 0.59 (15% EtOAc/hexane); ¹H NMR (CDCl₃, 270 MHz) δ 7.97 (d, J = 8.9 Hz, 2 H, ArH), 7.70 (t, J = 7.3 Hz, 1 H, ArH), 7.60 (t, J = 7.3 Hz, 2 H, ArH), 5.39 (t, J = 9.9 Hz, 1 H, H-2), 5.30 (d, J = 3.0 Hz, 1 H, H-4), 5.10 (dd, J = 9.9, 3.0 Hz, 1 H, H-3), 4.57 (d, J = 9.9 Hz, 1 H, H-1), 4.05-4.20 (m, 2 H, H-6), 3.79 (dd, J = 10.6, 5.9 Hz, 1 H, H-5), 1.25 (s, 9 H), 1.18 (s, 9 H), 1.08 (s, 9H), 0.92 (s, 9 H). ¹³C NMR (CDCl₃, 270 MHz) δ 177.7, 177.0, 176.7, 176.3, 134.4, 134.2, 131.0, 128.7, 89.4, 74.9, 71.7, 65.9, 63.9, 60.5, 38.4, 38.7, 38.6, 27.1.

To a solution of thioglycoside 40 (0.62 g, 1.0 mmol) in 20 mL of CH₂Cl₂ at -78 °C is added 67% m-CPBA (0.26 g, 1.0 mmol). The reaction mixture is stirred at

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-78 °C for 2 h and then allowed to slowly warm up to room temperature. Saturated NaHCO₃ is added until the solution is basic. The reaction mixture is diluted with 100 mL of CH₂Cl₂ and washed with H₂O (100 mL), saturated NaCl (100 mL), dried over Na₂SO₄, filtered, concentrated and purified by flash chromatography (15% EtOAc/hexane) to give 0.59 g (92%) of the title compound **41** as a mixture of diastereomers: R_f 0.38, 0.19 (20% EtOAc/hexane). FABMS $C_{32}H_{48}O_{10}S$ (MNa⁺) calcd 647.2866, found 647.2868.

7.21. 2,3,4,6-tetra-*O*-pivaloyl-1-deoxy-1-(phenylsulfinyl)-β-D-glucopyranose (45)

To a solution of D-glucose **42** (500 mg, 2.77 mmol) in 25 mL of pyridine is added pivaloyl chloride (3.42 mL, 3.34 g, 27.75 mmol) followed by DMAP (34 mg, 0.27 mmol). The reaction mixture is heated at 100 °C for 12 h, cooled to room temperature and quenched with 2 mL methanol. The reaction mixture is concentrated and the resulting residue is taken up in 25 mL CH₂Cl₂, washed with 1N HCl (3 x 25 mL), saturated NaCl (25 mL), dried over Na₂SO₄, filtered, concentrated and purified by flash chromatography (10% EtOAc/hexane) to afford 1.49 g (90%) of 1,2,3,4,6-penta-*O*-pivaloyl-β-D-glucopyranose **43**: R_f 0.18 (5% EtOAc/hexane); ¹H NMR (CDCl₃, 270 MHz) δ 5.69 (d, J = 8.2 Hz, 1H, H-1), 5.37 (app t, J = 9.2 Hz, 1H, H-3), 5.21 (app t, J = 8.7 Hz, 1H, H-4), 5.16 (app t, J = 9.5 Hz, 1H, H-2), 4.06-4.17 (m, 2H, H-6), 3.86 (ddd, J = 9.8, 4.8, 2.3 Hz, 1H, H-5), 1.21 (s, 9H), 1.17 (s, 9H), 1.15 (s, 9H), 1.12 (s, 18H).

To a solution of **43** (1.49 g, 2.49 mmol) in 50 mL CH₂Cl₂ is added thiophenol (0.64 mL, 686 mg, 6.22 mmol) followed by boron trifluoride diethyl ether complex (1.53 mL, 1.76 g, 12.45 mmol). The reaction mixture is stirred at room temperature for 4 h and

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quenched by the slow addition of 10 mL saturated NaHCO₃
solution. The reaction mixture is diluted with 100 mL
of CH₂Cl₂, washed with H₂O (100 mL), saturated NaCl (100
mL), dried over Na₂SO₄, filtered, concentrated and
purified by flash chromatography (5% EtOAc/hexane) to
afford 1.24 g (82%) of 1-deoxy-1-(phenylthio)-2,3,4,6-
tetra-O-pivaloyl-β-D-glucopyranose 44: R$_f$ 0.25 (5%
EtOAc/hexane); ¹H NMR (CDCl₃, 270 MHz) δ 7.47-7.50 (m,
2H), 7.22-7.30 (m, 3H), 5.34 (app t, J = 9.4 Hz, 1H, H-
3), 5.08 (app t, J = 9.7 Hz, 1H, H-4), 5.03 (app t, J =
9.7 Hz, 1H, H-2), 4.73 (d, J = 9.8 Hz, 1H, H-1), 4.25
(dd, J = 12.2, 1.6 Hz, 1H, H-6), 4.04 (dd, J = 12.2,
5.9 Hz, 1H, H-6), 3.76 (ddd, J = 10.2, 5.9, 1.6 Hz, 1H,
H-5), 1.21 (s, 9H), 1.20 (s, 9H), 1.14 (s, 9H), 1.10
(s, 9H); ¹³C NMR (CDCl3, 68 MHz) δ 177.8, 176.9, 176.2,
176.1, 132.5, 132.2, 129.2, 129.1, 128.1. 128.8, 86.4,
76.3, 73.1, 69.3, 67.5, 62.1, 38.7, 38.6, 27.4, 27.0,
29.9; FABMS C₃₂H₄₈O₉S (MNa⁺) calcd 631.2917, found
631.2943.

To a solution of 44 (1.24 g, 2.04 mmol) in 25
mL of CH₂Cl₂ at -78 °C is added a solution of 64% m-
CPBA (550 mg, 2.04 mmol) in 10 mL of CH₂Cl₂. The
reaction mixture is allowed to warm to -15 °C, quenched
with methyl sulfide (2.07 mL, 1.75 g, 6.8 mmol) and
warmed to room temperature. The reaction mixture is
then diluted with 25 mL CH₂Cl₂, washed with saturated
NaHCO₃ (50 mL), H₂O (50 mL), saturated NaCl (50 mL),
dried over Na₂SO₄, filtered, concentrated and purified
by flash chromatography (30% EtOAc/hexane) to afford
1.14 g (89%) of the title compound 45 as a mixture of
diastereomers: R$_f$ 0.14 and 0.28 (10% EtOAc/hexane).

7.22. 2,3,4,6-tetra-O-pivaloyl-1-deoxy-1-
(phenylsulfinyl)-β-L-glucopyranose (L-45)

By the method above, but beginning with L-
glucose, the title compound is prepared. To a solution

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of L-glucose L-42 (0.500 g, 2.77 mmol) in 25 mL of
pyridine is added pivaloyl chloride (3.4 mL, 27.8 mmol)
and DMAP (0.034 g, 0.27 mmol). The reaction mixture is
heated at 100 °C for 12 h, cooled to room temperature,
quenched with 2 mL of MeOH, and concentrated. The
resulting residue is taken up in 25 mL of CH_2Cl_2,
washed with 1N HCl (3 x 25 mL), saturated NaCl (25 mL),
dried over Na_2SO_4, filtered, concentrated, and purified
by flash chromatography (10% EtOAc/petroleum ether) to
afford 1.49 g (90%) of perpivolated glucose L-43. R_f
0.18 (5% EtOAc/petroleum ether); ^{1}H NMR ($CDCl_3$, 270
MHz) δ 5.69 (d, J = 8.2 Hz, 1H, H-1), 5.37 (app t, J =
9.4 Hz, 1H, H-3), 5.21 (app t, J = 8.7 Hz, 1H, H-4),
5.16 (app t, J = 9.5 Hz, 1H, H-2), 4.06-4.14 (m, 2H, H-
6), 3.86 (ddd, J = 9.8, 4.6, 2.3 Hz, 1H, H-5), 1.21 (s,
9H), 1.17 (s, 9H), 1.15 (s, 9H), 1.12 (s, 18H).

To a solution of perpivolated glucose (L-43) (1.49
g, 2.49 mmol) in 50 mL CH_2Cl_2 is added thiophenol (0.64
mL, 6.22 mmol) and $BF_3 \cdot Et_2O$ (1.5 mL, 12.5 mmol). The
reaction mixture is stirred at room temperature for 4
h, quenched with 10 mL of saturated $NaHCO_3$, diluted
with 100 mL of CH_2Cl_2, washed with H_2O (100 mL),
saturated NaCl (100 mL), dried over Na_2SO_4, filtered,
concentrated, and purified by flash chromatography (5%
EtOAc/petroleum ether) to afford 1.29 g (86%) of
glucose thioglycoside L-44: R_f 0.25 (5%
EtOAc/petroleum ether); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.46-
7.50 (m, 2H), 7.28-7.30 (m, 3H), 5.34 (app t, J = 9.3
Hz, 1H, H-3), 5.08 (app t, J = 9.7 Hz, 1H, H-4), 5.03
(app t, J = 9.7 Hz, 1H, H-2), 4.73 (d, J = 9.9 Hz, 1H,
H-1), 4.25 (dd, J = 12.1, 1.4 Hz, 1H, H-6), 4.05 (dd, J
= 12.2, 6.0 Hz, 1H, H-6), 3.76 (ddd, J = 9.9, 5.9, 1.4
Hz, 1H, H-5), 1.15 (s, 9H), 1.14 (s, 9H), 1.10 (s, 9H),
1.09 (s, 9H); FABMS $C_{32}H_{48}O_9S$ (MNa[+]) calcd 631.2917,
found 631.2952.

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To a solution of glucose thioglycoside L-44 (1.07 g, 1.76 mmol) in 25 mL of CH$_2$Cl$_2$ at -78 °C is added a solution of mCPBA (0.476 g, 1.76 mmol, 64% from Sigma) in 10 mL of CH$_2$Cl$_2$. The reaction mixture is allowed to warm to -15 °C, quenched using methyl sulfide (1.79 mL, 1.52 g, 5.9 mmol), warmed to room temperature. The reaction mixture is then diluted with 25 mL of CH$_2$Cl$_2$, washed with saturated NaHCO$_3$ (50 mL), H$_2$O (50 mL), saturated NaCl (50 mL), dried over Na$_2$SO$_4$, filtered, concentrated, and purified by flash chromatography (30% EtOAc/petroleum ether) to afford 0.977 g (89%) of sulfoxide **L-45** as a mixture of diastereomers: R$_f$ 0.10 and 0.18 (15% EtOAc/petroleum ether).

7.23.   4-*O*-(2,3,4,6-tetra-*O*-pivaloyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-pivaloyl-1-deoxy-1-phenylsulfinyl-β-D-glucopyranose (51)

To a solution of α-lactose monohydrate (**46**, 2.5 g, 6.9 mmol) in 45 mL of pyridine is added acetic anhydride (15 mL, 160 mmol) and DMAP (0.10 g, 0.82 mmol). The solution is stirred overnight and concentrated *in vacuo*. The residue is dissolved in 100 mL of CH$_2$Cl$_2$, washed with 1N HCl (3 x 50 mL), dried over Na$_2$SO$_4$, and concentrated to afford 4.7 g (100%) of octa-acetyl lactose **47** as the α anomer: R$_f$ 0.50 (75% EtOAc/hexane); ^{1}H NMR (CDCl$_3$, 270 MHz) δ 6.23 (d, J = 3.6 Hz, 1H, H-1), 5.44 (appt, J = 9.7 Hz, 1H), 5.34 (d, J = 2.6 Hz, 1H), 5.07-5.14 (m, 1H), 4.91-5.07 (m, 2H), 4.40-4.48 (m, 2H), 3.96-4.17 (m, 4H), 3.76-3.89 (m, 2H), 2.16 (s, 3H), 2.14 (s, 3H), 2.11 (s, 3H), 2.04 (s, 6H), 2.03 (s, 3H), 1.99 (s, 3H), 1.95 (s, 3H).

To a solution of octa-acetyl lactose **47** (4.7 g, 6.9 mmol) in 75 mL of CH$_2$Cl$_2$ is added thiophenol (1.42 mL, 13.9 mmol) followed by boron trifluoride diethyl ether complex (6.40 mL, 52.0 mmol). The reaction mixture is stirred at room temperature for 7 h and is

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then concentrated to half its volume by passing N₂ over
it for 3 h. The reaction is stirred an additional 16 h
at room temperature and then quenched by pouring slowly
into 150 mL of saturated aqueous $NaHCO_3$ and stirring
for 5 min. The product is extracted with CH_2Cl_2 (3 x
75 mL), dried over Na_2SO_4 and concentrated in vacuo to
an oil which is purified by flash chromotography to
give 4.1 g (81%) of the phenyl thioglycoside of hepta-
acetyl lactose **48** as a 5:1 (β:α) mixture of anomers:
R_f 0.34 (50% EtOAc/hexane); ¹H NMR ($CDCl_3$, 270 MHz) β-
anomer, δ 7.46-7.49 (m, 2H), 7.26-7.32 (m, 3H), 5.34
(d, J = 3.3 Hz, 1H), 5.22 (appt, J = 9.1 Hz, 1H), 5.07-
5.14 (m, 1H), 4.87-4.97 (m, 2H), 4.67 (d, J = 9.9 Hz,
1H), 4.45-4.56 (m, 2H), 4.03-4.16 (m, 3H), 3.86 (appt,
J = 6.8 Hz, 1H), 3.72-3.79 (m, 1H), 3.61-3.67 (m, 1H),
2.15 (s, 3H), 2.11 (s, 3H), 2.09 (s, 3H), 2.05 (s, 6H),
2.04 (s, 3H), 1.97 (s, 3H).

To a solution of acetylated phenyl
thioglycoside **48** (4.1 g, 5.6 mmol) in 80 mL of methanol
is added sodium methoxide (0.690 g, 12.8 mmol). The
solution is stirred for 2 h at room temperature.
Amberlite resin is added to the reaction mixture and
stirred for five min. The neutralized reaction mixture
is filtered through Celite and concentrated in vacuo.
The lactose phenyl thioglycoside **49** is taken on to the
next step without further purification.

Lactose phenyl thioglycoside 49 is dissolved in 80
mL of pyridine, and pivaloyl chloride (20 mL, 170 mmol)
and DMAP (0.10 g, 0.82 mmol) are added. The reaction
mixture is heated to 110 °C for 24 h. Additional
pivaloyl chloride (5 mL, 40 mmol) and DMAP (0.10 g,
0.82 mmol) are added. The reaction is heated for
another 24 h at 110 °C. The reaction is allowed to
cool, poured into 50 mL of methanol, and stirred for 30
min. EtOAc (500 mL) is added, and the organic layer is
washed with 1N HCl (6 X 100 mL) and saturated NaCl (3 X

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100 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The residue is purified by flash chromatography (10% EtOAc/hexane) to give 3.3 g (57%) of the phenyl thioglycoside of hepta-pivaloyl lactose 50 as a white foam, a 5:1 (β:α) mixture of anomers: R_f 0.23 (10% EtOAc/hexane); ^1H NMR ($CDCl_3$, 300 MHz) β-anomer, δ 7.45-7.49 (m, 2H), 7.26-7.31 (m, 3H), 5.40 (d, J = 2.6 Hz, 1H), 5.24 (appt, J = 9.4 Hz, 1H), 5.08-5.15 (m, 1H), 4.94-5.02 (m, 1H), 4.85 (appt, J = 9.6 Hz, 1H), 4.70 (d, J = 10.2 Hz, 1H), 4.49-4.59 (m, 2H), 3.82-4.24 (m, 5H), 3.55-3.61 (m, 1H), 1.27 (s, 9H), 1.22 (s, 9H), 1.21 (s, 9H), 1.19 (s, 9H), 1.18 (s, 9H), 1.13 (s, 9H), 1.09 (s, 9H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 177.9, 177.7, 177.4, 177.1, 177.0, 176.6, 176.1, 133.4, 132.0, 131.7, 129.3, 129.0, 128.5, 100.3, 86.3, 77.6, 73.5, 72.7, 71.8, 71.5, 70.0, 68.9, 67.0, 62.2, 61.4, 39.1, 39.1, 38.9, 27.6, 27.5, 27.4, 27.3; FABMS $C_{53}H_{82}O_{17}S$ (MNa$^+$) calcd 1045.5170, found 1045.5173.

To a solution of hepta-pivaloyl lactose phenyl thioglycoside 50 (2.0 g, 1.9 mmol) in 60 mL of CH_2Cl_2 at -78 °C is added 65% *m*-CPBA (0.546 g, 2.02 mmol). The reaction mixture is allowed to warm to -15 °C and quenched with methyl sulfide (0.3 mL, 4 mmol). The reaction mixture is then diluted with 100 mL of saturated $NaHCO_3$ and extracted with CH_2Cl_2 (2 X 100 mL). The organic layers are combined, dried over Na_2SO_4, and concentrated *in vacuo*. The product is purified by flash chromatography (25% EtOAc/hexane) to afford 2.0 g (100%) of the title compound 51 as a mixture of diastereomers: R_f 0.19 (20% EtOAc/hexane).

7.24.   4-*O*-(2,3,4,6-tetra-*O*-pivaloyl-α-D-glucopyranosyl)-2,3,6-tri-*O*-pivaloyl-1-deoxy-1-phenylsulfinyl-β-D-glucopyranose (53)

By the method above, but beginning with maltose monohydrate (52), the title compound is

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obtained as a mixture of diastereomers. To a solution
of maltose monohydrate 52 (3.5 g, 9.7 mmol) in 40 mL of
pyridine at room temperature is added acetic anhydride
(20 mL, 210 mmol) and DMAP (0.10 g, 0.82 mmol). The
solution is stirred at room temperature for 5 h and
concentrated. The residue is dissolved in 200 mL of
CH_2Cl_2, washed with 1N HCl (4 x 100 mL), dried over
Na_2SO_4, and concentrated to afford 6.6 g (100%) of
peracetylated maltose as the β anomer maltose-47: R_f
0.58 (75% EtOAc/petroleum ether); ^1H NMR (CDCl$_3$, 270
MHz) δ 5.74 (d, J = 8.2 Hz, 1H, H-1), 5.26-5.41 (m,
3H), 4.94-5.09 (m, 2H), 4.86 (dd, J = 10.5, 4.0 Hz,
1H), 4.45 (dd, J = 12.4, 2.3 Hz, 1H), 4.19-4.27 (m,
2H), 4.0-4.07 (m, 2H), 3.91-3.96 (m, 1H), 3.80-3.87 (m,
1H), 2.14 (s, 3H), 2.10 (s, 6H), 2.05 (s, 3H), 2.03 (s,
3H), 2.01 (s, 6H), 2.00 (s, 3H).

To a solution of peracetylated maltose maltose-47
(6.8 g, 10.0 mmol) in 70 mL of CH_2Cl_2 is added
thiophenol (2.1 mL, 20 mmol) followed by BF$_3$·Et$_2$O (9.2
mL, 75 mmol). The reaction mixture is stirred at room
temperature for 0.5 h, quenched with 100 mL of
saturated NaHCO$_3$, and extracted with CH_2Cl_2 (3 x 100
mL). Organic layers are combined, dried with Na_2SO_4,
concentrated, and purified by flash chromatography (40%
EtOAc/petroleum ether) to afford 6.4 g (88%) of maltose
thioglycoside maltose-48 as a 12:1 (β:α) mixture of
anomers: R_f 0.39 (50% EtOAc/petroleum ether); ^1H NMR
(CDCl$_3$, 270 MHz) β-anomer, δ 7.46-7.49 (m, 2H), 7.30-
7.33 (m, 3H), 5.39 (d, J = 4.3 Hz, 1H), 5.25-5.35 (m,
2H), 5.04 (appt, J = 9.9 Hz, 1H), 4.71-4.87 (m, 3H),
4.54 (dd, J = 12.0, 2.5 Hz, 1H), 3.91-4.27 (m, 5H),
3.70-3.75 (m, 1H), 2.13 (s, 3H), 2.10 (s, 3H), 2.07 (s,
3H), 2.04 (s, 3H), 2.03 (s, 3H), 2.00 (s, 3H), 1.99 (s,
3H).

To a solution of maltose thioglycoside maltose-48
(6.4 g, 8.8 mmol) in 100 mL of MeOH is added sodium

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methoxide (0.950 g, 17.6 mmol). The reaction mixture
is stirred at room temperature for 1.5 h, neutralized
with Amberlite IR-120 (plus) resin, filtered, washed
with MeOH, and concentrated to give the deprotected
intermediate maltose-49 which is taken on to the next
step without further purification.

To a solution of the intermediate maltose-49 in 75
mL of pyridine is added pivaloyl chloride (32.5 mL, 264
mmol) followed by DMAP (0.10 g, 0.82 mmol). The
reaction is heated at 110 °C. After 28 h, additional
pivaloyl chloride (8.0 mL, 65 mmol) is added, and the
reaction mixture is heated at 110 °C for 24 h. The
reaction mixture is allowed to cool, poured into 100 mL
of MeOH, diluted with 300 mL of EtOAc, washed with H_2O
(100 mL), 1N HCl (6 x 100 mL), saturated NaCl (3 x 100
mL), dried over Na_2SO_4, and concentrated. The residue
is purified by flash chromatography (1-5%
EtOAc/petroleum ether) to give 5.6 g (62%) of
perpivolated maltose maltose-50 as a 12:1 (β:α) mixture
of anomers as a white foam: R_f 0.38 (10%
EtOAc/petroleum ether); ^1H NMR (CDCl$_3$, 270 MHz) β-
anomer, δ 7.47-7.51 (m, 2H), 7.27-7.32 (m, 3H), 5.45
(appt, J = 9.7 Hz, 1H), 5.22-5.29 (m, 2H), 5.13 (app t,
J = 9.72 Hz, 1H), 4.72-4.89 (m, 3H), 4.59 (dd, J =
11.7, 2.5 Hz, 1H), 4.23 (dd, J = 11.9, 5.9 Hz, 1H),
4.09-4.14 (m, 2H), 4.01 (app t, J = 8.9 Hz, 1H), 3.88-
3.95 (m, 1H), 3.69-3.74 (m, 1H), 1.26 (s, 9H), 1.23 (s,
9H), 1.21 (s, 9H), 1.19 (s, 9H), 1.16 (s, 9H), 1.15 (s,
9H), 1.11 (s, 9H); ^{13}C NMR (CDCl$_3$, 68 MHz) δ 178.0,
177.8, 177.4, 177.1, 176.7, 176.6, 176.3, 132.9, 132.6,
132.1, 129.3, 129.1, 128.3, 93.2, 86.4, 76.7, 76.3,
70.5, 70.3, 69.6, 69.3, 68.7, 67.8, 63.1, 61.7, 39.1,
39.0, 38.9, 27.5, 27.4, 27.2, 27.0; FABMS $C_{53}H_{82}O_{17}S$
(MNa$^+$) calcd 1045.5170, found 1045.5121.

To a solution of perpivoated maltose maltose-50
(2.0 g, 1.9 mmol) in 60 mL of CH_2Cl_2 at -78 °C is added

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mCPBA (0.54 g, 2.0 mmol, 64%). The reaction is allowed
to warm to -15 °C, quenched with methyl sulfide (0.3
mL, 4 mmol), diluted with 100 mL of saturated NaHCO,,
and extracted with CH₂Cl₂ (2 x 100 mL). Organic layers
are combined, dried over Na₂SO₄, concentrated, and
purified by flash chromatography (20% EtOAc/petroleum
ether) to give 2.0 g (100%) of sulfoxide 53 as a
mixture of diastereomers as a white foam: R_f 0.31 (20%
EtOAc/petroleum ether).

7.25. 4-[(3-O-acetyl-2-azido-4,6-O-benzylidine-1,2-dideoxy-α-D-glucosyl)thio]phenoxyacetic acid (64)

To acetic anhydride (100 mL) is added
mannose (0.1 g) and concentrated perchloric acid (8
drops). The solution is heated to 30°C and mannose
(24.5 g, 136 mmol) is added in small portions over a
period of 2 h while the reaction temperature is kept
between 40-45 °C. The reaction mixture is allowed to
cool and then stirred for 3 h at room temperature to
produce crude mannose pentaacetate 54: R_f 0.31 (50%
EtOAc/hexane).

The reaction mixture is cooled at 10 °C and
phosphorous tribromide (21.0 mL, 220 mmol) is added.
To this solution, water (11 mL, 610 mmol) is added
dropwise so that the internal temperature of the
reaction mixture is maintained at 20-25 °C. After 30
minutes, the addition is complete, and the reaction
mixture is stirred at room temperature for 1.5 h.

The reaction mixture is cooled to 5 °C and a
solution of sodium acetate trihydrate (74.4 g, 547
mmol) in water (100 mL) is added dropwise over 30
minutes. Initially, the reaction is exothermic until
approximately one third of the aqueous sodium acetate
solution had been added. During the course of the
addition, the temperature of the reaction mixture is
maintained at 20-25 °C and then stirred at room

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temperature for 20 minutes. The reaction mixture is poured onto ice and extracted with $CHCl_3$ (3 x 120 mL), washed with water (300 mL), saturated $NaHCO_3$ (300 mL), dried over $MgSO_4$, filtered and concentrated to a yellow oil. The product is recrystallized from diethyl ether (200 mL) to afford 11.6 g (24%) of 1,3,4,6-tetra-O-acetyl-β-D-mannopyranose 55 as a white solid: R_f 0.39 (33% hexane/EtOAc); ^1H NMR ($CDCl_3$, 270 MHz) d 5.80 (t, J = 0.99 Hz, 1H, H-1), 5.39 (app t, J = 9.8 Hz, 1H, H-4), 5.05 (ddd, J = 9.8, 3.0, 0.99 Hz, 1H, H-3), 4.30 (ddd, J = 12.4, 4.9, 0.66, 1H, H-6), 4.20 (br s, 1H, H-2), 4.12 (dd, J = 12.5, 2.3 Hz, 1H, H-6), 3.78 (dddd, J = 9.7, 4.9, 2.3, 0.99 Hz, 1H, H-5), 2.18 (s, 3H), 2.12 (s, 3H), 2.05 (s, 3H), 2.10 (s, 3H).

To a solution of mannose tetraacetate 55 (1.50 g. 4.30 mmol) in 46 mL of CH_2Cl_2 is added pyridine (1.0 mL, 13 mmol). The solution is cooled to -25 °C and trifluoromethanesulfonic anhydride (1.8 mL, 2.98 g, 10.5 mmol) is added dropwise. The reaction mixture is stirred for 45 min at -25 °C and then diluted with 50 mL of CH_2Cl_2, washed with H_2O (100 mL), $NaHCO_3$ (100 mL), saturated NaCl (100 mL), dried over $MgSO_4$, filtered, and concentrated to afford an orange gel. The product is recrystallized from diethyl ether (25 mL) to afford 1.59 g (77%) of 1,3,4,6-tetra-O-acetyl-2-O-trifluoromethanesulfonyl-β-D-mannopyranose 56 as a white solid: R_f 0.49 (50% EtOAc/hexane); ^1H NMR ($CDCl_3$, 300 MHz) δ 5.92 (s, 1H, H-1), 5.15-5.34 (m, 3H), 4.15-4.28 (m, 2H), 3.81-3.87 (m, 1H, H-5), 2.08 (s, 3H), 2.10 (s, 3H), 2.12 (s, 3H), 2.16 (s,3H).

To a solution of mannose triflate 56 (1.28 g, 2.66 mmol) in 14 mL of DMF is added sodium azide (0.69 g, 10.5 mmol). The reaction mixture is heated at 40 °C for 1.75 h, cooled to room temperature, diluted with 100 mL of CH_2Cl_2, washed with H_2O (100 mL), saturated NaCl (100 mL), dried over $MgSO_4$, filtered, and

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concentrated to afford a yellow oil. The product is
purified by flash chromatography (33% EtOAc/hexane) to
afford 0.80 g (81%) of 2-azido-2-deoxy-1,3,4,6-tetra-O-
acetyl-β-D-glucopyranose 57: R$_f$ 0.31 (33%
EtOAc/hexane) δ 5.55 (d, J = 8.6 Hz, 1H, H-1), 5.01-
5.15 (m, 2H, H-3, H-4), 4.31 (dd, J = 12.7, 4.5 Hz, 1H,
H-6), 4.08 (d, J = 12.5 Hz, 1H, H-6), 3.77-3.84 (m, 1H,
H-5), 3.69 (app t, J = 9.1 Hz, 1H, H-2), 2.10 (s, 3H),
2.08 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H).

To a solution of 2-azido glucose tetraacetate 57
(0.222 g, 0.59 mmol) in 6.6 mL of CH$_2$Cl$_2$ is added 4-
hydroxythiophenol (0.146 g, 1.15 mmol) followed by
boron trifluoride diethyl ether complex (15.9 mL, 18.4
g. 141 mmol). The reaction mixture is heated at 45 °C
for 12 h and then quenched by the addition of 2 mL of
H$_2$O. The reaction mixture is diluted with 25 mL of
CH$_2$Cl$_2$, washed with H$_2$O (10 mL), saturated NaCl (10 mL),
dried over Na$_2$SO$_4$, filtered, and concentrated to afford
0.232 g of crude 2-azido-1,2-dideoxy-1-(4-
hydroxyphenylthio)-3,4,6-tri-O-acetyl-α,β-D-
glucopyranose 58 as a yellow oil, a mixture of anomers
which is then taken on to the next step without further
purification.

To a solution of the thioglycoside anomers 58 in
5.2 mL of methanol is added K$_2$CO$_3$ (0.146 g, 1.06 mmol).
The reaction mixture is stirred at room temperature for
10 min. Amberlite resin (acid form) is added to the
reaction mixture and stirred for an additional 15 min.
The neutralized mixture is then filtered through
Celite, washed several times with methanol, and
concentrated to afford 0.512 g of 2-azido-1,2-dideoxy-
1-(4-hydroxyphenylthio)-α,β-D-glucopyranose 59. The
product is purified by flash chromatography over silica
gel (10% MeOH in CH$_2$Cl$_2$) to afford 0.028 g (15% from
57) as a 2:1 (α, β) mixture of anomers: R$_f$ (α-anomer)
0.33 (10% MeOH/CH$_2$Cl$_2$); R$_f$ (β-anomer) 0.26 (10%

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MeOH/CH$_2$Cl$_2$); ^{1}H NMR (d$_6$-acetone, 270 MHz, mixture of
anomers) δ 8.69 (br s, 1H), 8.63 (br s, 1H), 7.45 (d, J
= 8.9 Hz, 2H), 7.40 (d, J = 8.6 Hz, 2H), 6.84 (d, J =
8.6 Hz, 2H), 6.81 (d, J = 8.6 Hz, 2H), 5.36 (d, J = 4.6
Hz, 1H), 4.85-4.89 (m, 2H), 4.55 (d, J = 5.3 Hz, 1H),
4.40 (d, J = 9.2 Hz, 1H), 4.43-4.45 (m, 2H), 4.11-4.18
(m, 1H), 3.42-3.88 (m, 7H), 3.27-3.37 (m, 4H), 3.08
(app t, J = 9.7 Hz, 1H).

To a solution of mixed anomers 59 (2.10 g, 6.70
mmol) in 85 mL of THF is added benzaldehyde dimethyl
acetal (3.0 mL, 3.10 g, 20.1 mmol) and camphorsulfonic
acid (0.31 g, 1.34 mmol). The reaction mixture is
stirred at 62 °C for 7 h and then at room temperature
for 10 h, cooled and concentrated to afford a brown
oil. The product is purified by flash chromatography
on silica gel (20% EtOAc/hexane) to afford 1.16 g (43%)
of 2-azido-4,6-O-benzylidene-1,2-dideoxy-1-(4-
hydroxyphenylthio)-α,β-D-glucopyranose 60 as a mixture
of anomers. The anomers are separable by flash
chromatography (20% EtOAc/hexane): R$_f$ (α-anomer) 0.31
(40% EtOAc/hexane); R$_f$ (β-anomer) 0.42 (40%
EtOAc/hexane); ^{1}H NMR (CDCl$_3$, 270 MHz) α-anomer, δ
7.33-7.55 (m, 7H), 6.84 (d, J = 8.9 Hz, 2H), 5.64 (s,
1H), 5.49 (d, J = 4.6 Hz, 1H, H-1), 4.32 (td, J = 9.8,
4.9 Hz, 1H, H-5), 4.16 (dd, J = 10.2, 4.9 Hz, 1H, H-6),
3.92-4.03 (m, 2H), 3.77 (app t, J = 10.2 Hz, 1H, H-6),
3.63 (app t, J = 9.3 Hz, 1H, H-4). The mixed anomers
are carried on to the following step without
separation.

To a solution of 4,6-benzylidene protected glucose
60 (1.04 g, 2.58 mmol) and 2-(trimethylsilyl)ethyl 2-
bromoacetate (1.27 g, 5.16 mmol) in 25 mL of DMF is
added K$_2$CO$_3$ (0.35 g, 2.58 mmol). The reaction mixture
is heated at 45 °C for 12 h, cooled, diluted with 50 mL
of CH$_2$Cl$_2$, washed with saturated NaHCO$_3$ (75 mL) and then
extracted with CH$_2$Cl$_2$ (2 x 50 mL), washed with H$_2$O (75

mL), saturated NaCl (75 mL), dried over Na₂SO₄,
filtered and concentrated to afford 5.40 g of the
anomers 61 and 62 of 2-(trimethylsilyl)ethyl 2-{4-[(2-
azido-4,6-O-benzylidene-1,2-dideoxy-D-
glucopyranosyl)thio]phenoxy}acetate. The anomers are
separated by flash chromatography (20% EtOAc/hexane) to
afford 0.811 g (56%) of α-anomer 61: R$_f$ 0.59 (40%
EtOAc/hexane), and 0.496 g (34%) of β-anomer 62: R$_f$
0.70 (40% EtOAc/hexane); ¹H NMR (CDCl₃, 300 MHz) α-
anomer, d 7.28-7.55 (m, 7H), 7.84 (d, J = 8.9 Hz, 2H),
5.50 (s, 1H), 5.36 (d, J = 5.5 Hz, 1H, H-1), 4.54 (s,
2H), 4.34 (td, J = 9.9, 4.7 Hz, 1H, H-5), 4.25 (m, 2H),
4.18 (dd, J = 10.4, 4.9 Hz, 1H, H-6), 3.97 (ddd, J =
9.9, 9.9, 1.8 Hz, 1H, H-3), 3.83 (dd, J = 9.8, 5.5 Hz,
1H, H-2), 3.69 (app t, J = 10.2 Hz, 1H, H-6), 3.51 (app
t, J = 9.3 Hz, 1H, H-4), 2.90 (br s, 1H), 1.0 (m, 2H),
0.50 (s, 9H); ¹H NMR (CDCl₃, 270 MHz) β-anomer, δ 7.33-
7.55 (m, 7H), 6.88 (d, J = 8.9 Hz, 2H), 5.52 (s, 1H),
4.62 (s, 2H), 4.43 (d, J = 10.2 Hz, 1H, H-1), 4.29-4.39
(m, 1H, H-6), 4.32 (m, 2H), 3.72-3.80 (m, 2H), 3.43-
3.48 (m, 2H), 3.30 (app t, J = 9.7 Hz, 1H, H-2), 1.02-
1.07 (m, 2H), 0.50 (s, 9H).

To a solution of 61 (0.848 g, 1.51 mmol) in 15 mL
of CH₂Cl₂ is added acetic anhydride (0.43 mL, 0.46 g,
4.54 mmol), triethylamine (0.63 mL, 0.46 g, 4.54 mmol),
and DMAP (0.187 g, 1.51 mmol). The reaction is stirred
at room temperature for 5 min and then diluted with 10
mL of CH₂Cl₂, washed with NaHCO₃ (15 mL), extracted with
CH₂Cl₂ (2 x 15 mL), washed with saturated NaCl (20 mL),
dried over Na₂SO₄, filtered and concentrated to afford
1.07 g of a yellow-orange oil. The product is purified
by flash chromatography (17% EtOAc/hexane) to afford
0.660 g (73%) of 2-(trimethylsilyl)ethyl 2-{4-[(3-O-
acetyl-2-azido-4,6-O-benzylidene-1,2-dideoxy-α-D-
glucopyranosyl)thio]phenoxy}acetate 63: R$_f$ 0.18 (17%
EtOAc/hexane); ¹H NMR (CDCl₃, 270 MHz) δ 7.29-7.43 (m,

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7H), 6.81 (d, J = 8.9 Hz, 2H), 5.39-5.46 (m, 3H), 4.44
(td, J = 9.9, 4.9 Hz, 1H, H-5), 4.24 (m, 2H), 4.18 (dd,
J = 10.2, 4.9 Hz, 1H, H-6), 3.96 (dd, J = 10.2, 5.6 Hz,
1H, H-2), 3.71 (app t, J = 10.2 Hz, 1H, H-6), 3.60 (app
t, J = 9.6 Hz, 1H, H-4), 2.11 (s, 3H), 1.0 (m, 2H),
0.87 (s, 9H).

To a solution of **63** (0.044 g, 0.073 mmol) in 0.4
mL of THF is added tetra-*n*-butylammonium fluoride
solution (1.0 M in THF, 0.36 mL, 0.36 mmol). The
reaction mixture is stirred for 20 min at room
temperature and diluted with 3 mL of CH_2Cl_2, washed
with 5% HCl (5 mL), extracted with CH_2Cl_2 (2 x 2 mL),
washed with saturated NaCl (5 mL), dried over Na_2SO_4,
filtered, and concentrated to afford 0.067 g of a clear
oil. The product is purified by flash chromatography
(2% $MeOH/CHCl_3$) to afford 0.035 g (95%) of 2-{4-[(3-*O*-
acetyl-2-azido-4,6-*O*-benzylidene-1,2-dideoxy-α-D-
glucopyranosyl)thio]phenoxy}acetic acid **64** as a white
solid: R_f 0.39 (5% $MeOH/CHCl_3$); ^{1}H NMR ($CDCl_3$, 270 MHz)
δ 7.35-7.49 (m, 7H), 6.90 (d, J = 8.9 Hz, 2H), 5.45-
5.52 (m, 3H), 4.69 (s, 2H), 4.48 (td, J = 9.8, 5.2 Hz,
1H, H-5), 4.24 (dd, J = 10.4, 4.7 Hz, 1H, H-6), 4.03
(dd, J = 10.2, 5.6 Hz, 1H, H-2), 3.78 (app t, J = 10.3
Hz, 1H, H-6), 3.67 (app t, J = 9.6 Hz, 1H, H-4), 2.15
(s, 3H). FABMS $C_{23}H_{23}O_8N_3S$ calcd 524.1104, found
524.1118.

7.26. 2-{4-[(3-*O*-acetyl-2-azido-4,6-*O*-benzylidine-1,2-dideoxy-β-D-glucosyl)thio]-phenoxy}acetic acid (66)

To a solution of **62** (0.496 g, 0.886 mmol)
in 10 mL of CH_2Cl_2 is added acetic anhydride (0.25 mL,
0.27 g, 2.65 mmol), triethylamine (0.37 mL, 0.27 g,
2.65 mmol), and DMAP (0.108 g, 0.886 mmol). The
reaction is stirred at room temperature for 20 min and
then diluted with 3 mL of CH_2Cl_2, washed with $NaHCO_3$ (10

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mL), extracted with CH_2Cl_2 (2 x 3 mL), washed with
saturated NaCl (5 mL), dried over Na_2SO_4, filtered and
concentrated to afford 0.612 g of a yellow oil. The
product is purified by flash chromatography (17%
EtOAc/hexane) to afford 0.438 g (82%) of 2-
(trimethylsilyl)ethyl 2-{4-[(3-O-acetyl-2-azido-4,6-O-
benzylidene-1,2-dideoxy-β-D-glucopyranosyl)thio]-
phenoxy}acetate 65: R_f 0.56 (40% EtOAc/hexane); ^1H NMR
($CDCl_3$, 300 MHz) δ 7.27-7.55 (m, 7H), 6.85 (d, J = 8.8
Hz, 2H), 5.41 (s, 1H), 5.17 (app t, J = 9.4Hz, 1H, H-
3), 4.57 (s, 2H), 4.43 (d, J = 10.3 Hz, 1H, H-1), 4.30-
4.34 (m, 1H), 4.26 (m, 2H), 3.70 (ddd, J = 10.3, 9.9,
2.7 Hz, 1H, H-5), 3.40-3.49 (m, 2H, H-4, H-6), 3.29
(app t, J = 9.7 Hz, 1H, H-2), 2.24 (s, 3H), 0.99 (m,
2H), 0.01 (s, 9H).

To a solution of 65 (0.425 g, 0.706 mmol) in 7 mL
of THF is added tetra-n-butylammonium fluoride solution
(1.0 M in THF, 3.5 mL, 3.53 mmol). The reaction
mixture is stirred for 5 min at room temperature and
diluted with 10 mL of CH_2Cl_2, washed with 5% HCl (10
mL), extracted with CH_2Cl_2 (2 x 5 mL), washed with
saturated NaCl (10 mL), dried over Na_2SO_4, filtered,
and concentrated to afford 0.65 g of a clear oil. The
product is purified by flash chromatography (gradient
elution: 50% EtOAc/hexane, 100% EtOAc, 20% MeOH/$CHCl_3$)
to afford 0.30 g (85%) of the title compound 66 as a
white solid: R_f 0.48 (5% MeOH/$CHCl_3$); ^1H NMR (C_6D_6, 300
MHz) δ 7.34-7.62 (m, 7H), 7.05 (d, J = 8.8 Hz, 2H),
5.67 (s, 1H), 5.34 (app t, J = 9.3 Hz, 1H, H-3), 4.92
(d, J = 10.3 Hz, 1H, H-1), 4.77 (s, 2H), 4.36 (dd, J =
9.3, 3.5 Hz, 1H), 3.70-3.90 (m, 3H), 3.52 (app t, J =
9.9 Hz, 1H, H-2), 2.05 (s, 3H); ^{13}C NMR (CD_3OD, 68 MHz)
δ 171.3, 160.1, 138.5, 137.2, 129.8, 128.9, 127.1,
122.7, 116.2, 102.4, 87.5, 79.3, 74.3, 71.4, 69.1,
65.2, 64.5, 20.6; FABMS $C_{23}H_{23}O_8N_3S$ (MNa$^-$) calcd
524.1104, found 524.1134.

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7.27.   2-{4-[(3-O-acetyl-2-azido-4,6-O-
        benzylidene-1,2-dideoxy-β-D-
        galactopyranosyl)thio]phenoxy}acetic acid
        (76).

To a solution of tri-O-acetyl-D-galactal **67**
(25.0 g, 91.8 mmol) in 1000 mL of distilled CH_3CN at -
20 °C is added sodium azide (8.96 g, 138 mmol),
followed by ceric ammonium nitrate (151 g, 276 mmol).
The reaction suspension is stirred vigorously at -15 to
-20 °C for 24 h and then filtered through Celite.   The
filtrate is diluted with 1000 mL of ice water and
extracted with CH_2Cl_2 (3 x 200 mL).   The combined
organic layers are dried over Na_2SO_4, concentrated, and
purified by flash chromatography (10% EtOAc/hexane) to
give 17.5 g (51%) of 2-azido-2-deoxy-1-O-nitro-3,4,6-
tri-O-acetyl-α,β-D-galactopyranose **68** as a mixture of
anomers: R_f 0.26 (25% EtOAc/hexane); ^1H NMR ($CDCl_3$, 270
MHz, mixture of anomers) δ 6.32 (d, J = 4.0 Hz, 1 H,
H-1α), 5.55 (d, J = 8.9 Hz, 1 H, H-1β), 5.48 (d, J =
3.0 Hz, 1 H, H-4α), 5.37 (d, J = 3.0 Hz, 1 H, H-4β),
5.23 (dd, J = 11.6, 3.3 Hz, 1 H, H-3α), 4.93 (dd, J =
10.6, 3.3 Hz, 1 H, H-3β), 4.35 (t, J = 6.6 Hz, 1 H, H-
5α), 3.9-4.2 (m, 6 H, H-2α, H-5β, H-6β, H-6α), 3.81
(dd, J = 10.6, 8.9 Hz, 1 H, H-2β), 1.95-2.25 (6s,18 H).

To a solution of nitrate ester **68** (17.5 g, 46.5
mmol) in 500 mL of glacial acetic acid is added sodium
acetate (7.63 g, 93.0 mmol).   The solution is stirred
at 100 °C for 3 h and then allowed to cool to room
temperature.   The reaction mixture is diluted with 1000
mL of ice water and extracted with CH_2Cl_2 (2 x 200 mL).
The organic layers are combined and washed with ice
water (2 x 400 mL), saturated $NaHCO_3$ (400 mL),
saturated NaCl (400 mL), dried over Na_2SO_4, filtered
and concentrated.   The crude product is crystallized
from hexane/EtOAc to give 7.2 g of 2-azido-2-deoxy-
1,3,4,6-tetra-O-acetyl-α,β-D-galactopyranose **69** (mixed
anomers).   The mother liquors from the crystallization

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are concentrated and purified by flash chromatography
(25% EtOAc/hexane) to give an additional 7.0 g of the
product (14.2 g, 81.7% in total) as a mixture of
anomers: R_f 0.3 (30% EtOAc/hexane); ^{1}H NMR (CDCl$_3$, 270
MHz, mixture of anomers) δ 6.26 (d, J = 3.6 Hz, 1 H, H-
1α), 5.50 (d, J = 8.6 Hz, 1 H, H-1β), 5.42 (d, J = 3.0
Hz, 1 H, H-4α), 5.32 (d, J = 3.0 Hz, 1 H, H-4β), 5.25
(dd, J = 11.2, 3.0 Hz, 1 H, H-3α), 4.85 (dd, J = 10.6,
3.3 Hz, 1 H, H-3β), 4.23 (t, J = 6.6 Hz, 1 H, H-5α),
3.95-4.10 (m, 5 H, H-6α, H-5β, H-6β), 3.88 (dd, J =
11.2, 3.6 Hz, 1 H, H-2α), 3.78 (dd, J = 10.9, 8.6 Hz, 1
H, H-2β), 1.90-2.20 (6s, 24 H, OAc).

To a solution of **69** (1.16 g, 2.95 mmol) in 100 mL
of CH$_2$Cl$_2$ is added 4-hydroxythiophenol (0.90 g, 5.9
mmol), followed by boron trifluoride diethyl ether
complex (1.5 mL, 11.8 mmol). The mixture is refluxed
at 50 °C for 48 h and then quenched by the addition of
200 mL of H$_2$O. The reaction mixture is diluted with
200 mL of CH$_2$Cl$_2$. The organic layer is washed with H$_2$O
(200 mL), saturated NaHCO$_3$ (2 x 200 mL), dried over
Na$_2$SO$_4$, filtered, and concentrated to give 2-azido-1,2-
dideoxy-1-(4-hydroxyphenylthio)-3,4,6-tri-O-acetyl-α,β-
D-galactopyranose **70** as a brown oil, R_f 0.13 (30%
EtOAc/hexane, which is taken on to the next reaction
without further purification. A purified sample of the
β-anomer had ^{1}H NMR (CDCl$_3$, 270 MHz) δ 7.51 (d, J = 8.9
Hz, 2 H, ArH), 6.82 (d, J = 8.9 Hz, 2 H, ArH), 5.33
(dd, J = 3.3, 1.0 Hz, 1 H, H-4), 5.08 (s, 1 H, ArOH),
4.85 (dd, J = 10.2, 3.3 Hz, 1 H, H-3), 4.24 (d, J =
10.2 Hz, 1 H, H-1), 4.17 (dd, J = 11.2, 6.6 Hz, 1 H, H-
6), 4.09 (dd, J = 11.2, 6.6 Hz, 1 H, H-6′), 3.85 (dt, J
= 6.6, 1.0 Hz, 1 H, H-5), 3.57 (t, J = 10.2 Hz, 1 H, H-
2), 2.08 (s, 3 H, OAc), 2.04 (s, 3 H, OAc), 2.03 (s, 3
H, OAc).

To a solution of **70** in 50 mL of MeOH is added
K$_2$CO$_3$ until pH paper indicated the solution to be basic

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(pH 11). The reaction mixture is stirred at room
temperature for 15 min and then neutralized with
Amberlite resin (acid form). The resin is removed by
filtration and washed with MeOH (2 x 50 mL). The
filtrates are concentrated and purified by flash
chromatography (70% EtOAc/hexane) to give 0.65 g (63%)
of 2-azido-1,2-dideoxy-1-(4-hydroxyphenylthio)-α,β-D-
galactopyranose 71: R_f 0.19 (100% EtOAc).

To a solution of 71 (1.20 g, 3.65 mmol) in 100 mL
of DMF is added benzaldehyde dimethyl acetal (1.65 mL,
10.9 mmol) and p-toluenesulfonic acid (0.14 g, 0.73
mmol). The reaction is stirred at room temperature for
8 h and then neutralized with saturated $NaHCO_3$. The
reaction mixture is diluted with 200 mL of EtOAc,
washed with saturated NaCl (3 x 200 mL), dried over
Na_2SO_4, filtered, concentrated and purified by flash
chromatography (35% EtOAc/hexane) to give 1.30 g (89%)
of 2-azido-4,6-O-benzylidene-1,2-dideoxy-1-(4-
hydroxyphenylthio)-α,β-D-galactopyranose 72. The mixed
anomers are used directly for the next step, although
the anomers are separable by flash chromatography (35%
EtOAc/hexane): R_f (α-anomer) 0.28 (40% EtOAc/hexane);
R_f (β-anomer) 0.11 (40% EtOAc/hexane); ^{1}H NMR (CDCl$_3$,
270 MHz) β-anomer, δ7.61 (d, J = 8.6 Hz, 2 H, ArH),
7.37-7.39 (m, 5 H, ArH), 6.76 (d, J = 8.6 Hz, 2 H,
ArH), 5.51 (s, 1 H, CH), 4.96 (s, 1 H, ArOH), 4.38 (dd,
J = 12.5, 1.7 Hz, 1 H, H-6), 4.32 (d, J = 9.6 Hz, 1 H,
H-1), 4.17 (d, J = 3.6 Hz, 1 H, H-4), 4.02 (dd, J =
12.5, 1.7 Hz, 1 H, H-6'), 3.65 (dt, J = 9.6, 3.6 Hz, 1
H, H-3), 3.51 (d, J = 1.3 Hz, 1 H, H-5), 3.45 (t, J =
9.6 Hz, 1 H, H-2), 2.50 (d, J = 9.9 Hz, 1 H, OH-3); α-
anomer, δ7.36-7.50 (m, 7 H, ArH), 6.77-6.80 (m, 2 H,
ArH), 5.61 (s, 1 H, CH), 5.57 (d, J = 5.3 Hz, 1 H, H-
1), 4.82 (s, 1 H, ArOH), 4.34 (dd, J = 3.6, 1.0 Hz, 1
H, H-4), 4.30 (d, J = 1.0 Hz, 1 H, H-5), 4.11-4.30 (m,
3 H, H-6, H-6'), 4.17 (dd, J = 10.2, 5.3 Hz, 1 H, H-2),

4.00 (dt, J =10.2, 3.5 Hz, 1 H, H-3), 2.52 (d, J = 10.2 Hz, 1 H, OH-3).

To a solution of **72** (1.70 g, 4.20 mmol) in 60 mL of DMF is added K_2CO_3 (0.58 g, 4.2 mmol) and 2-(trimethylsilyl)ethyl bromoacetate (2.0 g, 8.5 mmol). The reaction mixture is stirred at 50-60 °C for 3 h and then allowed to cool to room temperature. The reaction mixture is diluted with EtOAc (150 mL), washed with H_2O (3 x 80 mL) and saturated NaCl (80 mL), dried over Na_2SO_4, concentrated and purified by flash chromatography (45% EtOAc/hexane) to give 1.60 g (68%) of 2-(trimethylsilyl)ethyl 2-{4-[(2-azido-4,6-O-benzylidene-1,2-dideoxy-α,β-D-galactopyranosyl)thio]-phenoxy}acetate **73** as a mixture of anomers. The mixed anomers are used directly for the next step, but could be separated by flash chromatography (25% EtOAc/hexane to elute the α-anomer, 45% EtOAc/hexane to elute the β-anomer): R_f (α-anomer) 0.15 (25% EtOAc/hexane); R_f (β-anomer) 0.12 (35% EtOAc/hexane); ^{1}H NMR (CDCl$_3$, 270 MHz) α-anomer, δ 7.38-7.48 (m, 7 H, ArH), 6.86 (d, J = 8.8 Hz, 2 H, ArH), 5.61 (s, 1 H, CH), 5.59 (d, J = 5.5 Hz, 1 H, H-1), 4.59 (s, 2 H, OCH$_2$CO), 3.96-4.33 (m, 8 H, H-2, H-3, H-4, H-5, H-6, H-6', COOCH$_2$), 1.06 (t, J = 8.8 Hz, 2 H, CH$_2$TMS), 0.05 (s, 9 H, SiMe$_3$); β-anomer, δ 7.66 (d, J = 8.8 Hz, 2 H, ArH), 7.39 (s, 5 H, ArH), 6.82 (d, J = 9.2 Hz, 2 H, ArH), 5.52 (s, 1 H, CH), 4.55 (s, 2 H, OCH$_2$CO), 4.28-4.39 (m, 5 H, H-1, H-3, H-6, COOCH$_2$), 4.16 (d, J = 3.3 Hz, 1 H, H-4), 4.02 (d, J = 12.5 Hz, 1 H, H-6'), 3.49 (s, 1 H, H-5), 3.45 (t, J = 9.9 Hz, 1 H, H-2), 1.04 (t, J = 8.8 Hz, 2 H, CH$_2$TMS), 0.05 (s, 9 H, SiMe$_3$).

To a solution of **73** (1.60 g, 2.86 mmol) in 50 mL of CH$_2$Cl$_2$ is added Et$_3$N (0.8 mL, 2.86 mmol), acetic anhydride (0.6 mL, 5.72 mmol) and DMAP (0.35 g, 2.86 mmol). The reaction mixture is stirred at room temperature for 15 min. The reaction is diluted with

100 mL of CH_2Cl_2 and washed with saturated $NaHCO_3$ (80 mL), dried over Na_2SO_4, filtered, concentrated and purified by flash chromatography to give a combined yield of 1.31 g (76.4%) of the anomers of 2-(trimethylsilyl)ethyl 2-{4-[(3-O-acetyl-2-azido-4,6-O-benzylidene-1,2-dideoxy-α,β-D-galactopyranosyl)thio]-phenoxy}acetate (15% EtOAc/hexane to elute the α-anomer 75, 35% EtOAc/hexane to elute the β-anomer 74).

74: R_f 0.31 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$, 270 MHz), δ 7.65 (d, J = 8.8 Hz, 2 H, ArH), 7.39 (s, 5 H, ArH), 6.77 (d, J = 8.8 Hz, 2 H, ArH), 5.47 (s, 1 H, CH), 4.80 (dd, J = 10.6, 3.3 Hz, 1 H, H-3), 4.52 (s, 2 H, OCH$_2$CO), 4.42 (d, J = 9.9 Hz, 1 H, H-1), 4.36 (d, J = 12.1 Hz, 1 H, H-6), 4.31 (t, J = 8.8, 8.4 Hz, 2 H, COOCH$_2$), 4.29-4.31 (m, 1 H, H-4), 4.00 (d, J = 12.8 Hz, 1 H, H-6'), 3.76 (t, J = 10.6, 9.9 Hz, 1 H, H-2), 3.54 (s, 1 H, H-5), 2.10 (s, 3 H, OAc), 1.04 (t, J = 8.8, 8.4 Hz, 2 H, CH$_2$TMS), 0.06 (s, 9 H, SiMe$_3$);

75: R_f 0.38 (25% EtOAc/hexane); ^{1}H NMR ($CDCl_3$, 270 MHz), δ 7.33-7.49 (m, 5 H, ArH), 7.39 (d, J = 8.9 Hz, 2 H, ArH), 6.83 (d, J = 8.9 Hz, 2 H, ArH), 5.61 (d, J = 5.3 Hz, 1 H, H-1), 5.52 (s, 1 H, CH), 5.01 (dd, J = 11.2, 3.6 Hz, 1 H, H-3), 4.56 (s, 2 H, OCH$_2$CO), 4.49-4.55 (m, 2 H, H-2, H-4), 4.28 (m, 2 H, COOCH$_2$), 4.24 (br s, 1 H, H-5), 4.18(dd, J = 12.5, 1.3 Hz, 1 H, H-6), 4.07 (dd, J = 12.5, 1.3 Hz, 1 H, H-6'), 2.14 (s, 3 H, OAc), 1.01 (m, 2 H, CH$_2$TMS), 0.03 (s, 9 H, SiMe$_3$); ^{13}C NMR ($CDCl_3$, 270 MHz), δ 170.4, 168.8, 158.0, 137.5, 134.3, 129.2, 128.3, 126.2, 124.9, 115.6, 100.9, 88.3, 73.3, 71.4, 69.2, 65.6, 64.0, 63.4, 57.9, 21.1, 17.5, -1.35.

To a solution of 74 (0.628 g, 1.04 mmol) in 10 mL of THF is added tetra-n-butylammonium fluoride (2.1 mL of 1.0 M solution in THF, 2.09 mmol). The reaction mixture is stirred at room temperature for 10 min and then neutralized with dilute HCl, concentrated and

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purified by flash chromatography (0.1% HOAc, 5% MeOH, in EtOAc) to give 0.486 g (93%) of the title compound 76: R_f 0.14 (10% MeOH/EtOAc); ^{1}H NMR (CDCl$_3$, 270 MHz) δ 7.64 (d, J = 8.6 Hz, 2 H, ArH), 7.37 (s, 5 H, ArH), 6.73 (d, J = 8.9 Hz, 2 H, ArH), 5.45 (s, 1 H, CH), 4.81 (dd, J = 10.2, 3.0 Hz, 1 H, H-3), 4.53 (s, 2 H, OCH$_2$CO), 4.42 (d, J = 9.9 Hz, 1 H, H-1), 4.33 (d, J = 11.9 Hz, 1 H, H-6), 4.28 (d, J = 3.0 Hz, 1 H, H-4), 3.96 (d, J = 11.9 Hz, 1 H, H-6'), 3.75 (t, J = 10.2, 9.9 Hz, 1 H, H-2), 3.50 (s, 1 H, H-5), 2.08 (s, 3 H, OAc). ^{13}C NMR (CDCl$_3$, 270 MHz) δ 173.4, 170.7, 158.2, 137.6, 136.6, 129.3, 128.3, 126.4, 121.9, 115.3, 100.7, 85.3, 74.0, 72.7, 69.5, 69.2, 64.8, 58.3, 21.1.

7.28.   2-{4-[(3-O-acetyl-2-azido-4,6-O-benzylidene-1,2-dideoxy-α-D-galactopyranosyl)thio]phenoxy}acetic acid (77)

The title compound is prepared from 75 by treatment with tetrabutylammonium fluoride, and purified by flash chromatography, as described above: R_f 0.14 (30% MeOH/EtOAc); ^{1}H NMR (CDCl$_3$, 270 MHz) δ 7.44-7.48 (m, 2 H, ArH), 7.33-7.38 (m, 5 H, ArH), 6.80 (d, J = 8.6 Hz, 2 H, ArH), 5.61 (d, J = 4.9 Hz, 1 H, H-1), 5.49 (s, 1 H, CH), 4.48-4.56 (m, 4 H, H-2, H-4, OCH$_2$CO), 5.10 (dd, J = 10.9, 3.3 Hz, 1 H, H-3), 4.21 (s, 1 H, H-5), 4.14 (d, J = 12.9 Hz, 1 H, H-6), 4.04 (d, J = 12.2 Hz, 1 H, H-6'), 2.16 (s, 3 H, OAc). ^{13}C NMR (CDCl$_3$, 270 MHz) δ 173.9, 170.6, 157.7, 137.5, 134.5, 129.3, 128.3, 126.3, 125.2, 115.7, 100.9; 88.2, 73.3, 71.5, 69.2, 65.3, 63.5, 57.9, 21.1.

7.29.   2-{4-[(3-O-acetyl-4-azido-2,6-bis-O-(4-methoxybenzyl)-1,4-dideoxy-β-D-glucopyranosyl)thio]phenoxy}acetic acid (88)

To a solution of galactose pentaacetate
(3.30 g, 8.50 mmol) and 4-hydroxy-thiophenol (1.40 g,
11.1 mmol) in 50 mL of methylene chloride at -78 °C is
added boron trifluoride diethyl ether complex (2.10 mL,
17.1 mmol). The solution is allowed to warm slowly to
0 °C and then stirred for an additional hour at 0 °C.
The mixture is poured into saturated aqueous $NaHCO_3$
(200 mL) and extracted with CH_2Cl_2 (2 x 150 mL), dried
over Na_2SO_4, concentrated, and purified by flash
chromatography (50% EtOAc/hexane) to give 3.90 g (99%)
of 1-deoxy-1-(4-hydroxyphenylthio)-2,3,4,6-tetra-O-
acetyl-β-D-galactopyranose 78 as a white solid: R_f 0.3
(50% EtOAc/hexane); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.42 (d,
J = 8.6 Hz, 2H), 6.79 (d, J = 8.6 Hz, 2H), 5.78 (br s,
1H), 5.39 (d, J = 2.56 Hz, 1H, H-4), 5.15 (t, J = 9.9
Hz, 1H, H-2), 5.00 (dd, J = 3.3, 9.9 Hz, 1H, H-3), 4.56
(d, J = 9.9 Hz, 1H, H-1), 4.19 (dd, J = 6.6, 11.0 Hz,
1H), 4.09 (dd, J = 6.6, 11.0 Hz, 1H), 3.89 (t, J = 6.6
Hz, 1H, H-5), 2.12 (s, 3H, OAc), 2.09 (s, 3H, OAc),
2.05 (s, 3H, OAc), 1.97 (s, 3H, OAc).

To a solution of thioglycoside 78 (1.40 g, 3.10
mmol) in 15 mL of methylene chloride is added N,N-
diisopropylethylamine (0.64 mL, 3.70 mmol), followed by
2-(trimethylsilyl)ethoxymethyl chloride (0.60 mL, 3.40
mmol). The mixture is stirred at room temperature for
2 h, poured into saturated NaCl (50 mL) and extracted
with CH_2Cl_2 (2 x 50 mL), dried over Na_2SO_4,
concentrated, and purified by flash chromatography (40%
EtOAc/hexane) to give 1.60 g (89%) of 1-deoxy-1-{4-[2-
(trimethylsilyl)ethoxymethoxy]phenylthio}-2,3,4,6-
tetra-O-acetyl-β-D-galactopyranose 79 as a colorless
oil: R_f 0.4 (33% EtOAc/hexane); ^{1}H NMR ($CDCl_3$, 270 MHz)
δ 7.46 (d, J = 8.4 Hz, 2H), 6.98 (d, J = 8.4 Hz, 2H),
5.40 (d, J = 3.3 Hz, 1H, H-4), 5.22 (s, 2H, SEM), 5.20
(dd, J = 9.9, 9.9 Hz, 1H, H-2), 5.02 (dd, J = 3.3, 9.9
Hz, 1H, H-3), 4.58 (d, J = 9.9 Hz, 1H, H-1), 4.18 (dd,

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J = 6.6, 11.2 Hz, 1H), 4.10 (dd, J = 6.6, 11.2 Hz, 1H),
3.89 (dd, J = 6.6, 6.6 Hz, 1H, H-5), 3.75 (t, J = 8.4
Hz, 2H, SEM), 2.11 (s, 3H, OAc), 2.10 (s, 3H, OAc),
2.04 (s, 3H, OAc), 1.98 (s, 3H, OAc), 0.94 (t, J = 8.4
Hz, 2H, CH_2-TMS), 0.01 (s, 9H, $SiMe_3$).

To a solution of the SEM protected thioglycoside
79 (1.60 g, 2.73 mmol) in 15 mL of methanol is added
sodium methoxide (300 mg, 5.56 mmol). The mixture is
stirred at room temperature for 12 h, then neutralized
with Amberlite resin (acid form), filtered,
concentrated and run through a short column of silica
gel (10% MeOH/EtOAc) to provide crude 1-deoxy-1-{4-[2-
(trimethylsilyl)ethoxymethoxy]phenylthio}-β-D-
galactopyranose 80 as an oil: R_f 0.15 (EtOAc). The
material is taken up in 10 mL of DMF, and
dimethoxypropane (0.59 mL, 4.8 mmol), and p-
toluenesulfonic acid hydrate (90 mg, 0.48 mmol) are
added. The mixture is stirred at room temperature for
12 h, pyridine (0.04 mL, 0.48 mmol) is added, and the
reaction mixture is concentrated and purified by flash
chromatography (60% EtOAc/hexane) to give 0.5 g (41%)
of 1-deoxy-3,4-O-isopropylidene-1-{4-[2-
(trimethylsilyl)ethoxymethoxy]phenylthio}-β-D-
galactopyranose 81 as a colorless oil: R_f 0.5 (67%
EtOAc/hexane); ^{1}H NMR (CDCl$_3$, 300 MHz) δ 7.48 (d, J =
8.6 Hz, 2H), 6.99 (d, J = 8.6 Hz, 2H), 5.21 (s, 2H,
SEM), 4.35 (d, J = 10.2 Hz, 1H, H-1), 4.17 (dd, J =
1.7, 5.4 Hz, 1H), 4.09 (dd, J = 6.5 Hz, 1H), 3.94 (m,
1H), 3.85 (m, 2H), 3.73 (t, J = 8.1 Hz, 2H, SEM), 3.52
(m, 1H), 2.49 (d, J = 1.8 Hz, 1H), 2.17 (d, J = 9.1 Hz,
1H), 1.40 (s, 3H, Me), 1.33 (s, 3H, Me), 0.93 (t, J =
8.1 Hz, 2H, CH_2-TMS), 0.01 (s, 9H, $SiMe_3$).

To a solution of acetonide 81 (80 mg, 0.175 mmol)
in 3 mL of DMF is added tetrabutylammonium iodide (194
mg, 0.52 mmol), 4-methoxybenzyl choride (0.19 mL, 1.40
mmol), and a 95% dispersion of sodium hydride (11 mg,

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0.44 mmol). The mixture is stirred at room temperature for 1 h, then poured into saturated NaHCO₃ (30 mL) and extracted with CH_2Cl_2 (2 x 30 mL), dried over Na_2SO_4, concentrated, and purified by flash chromatography (25% EtOAc/hexane) to give 98 mg (87%) of 2,6-bis-O-(4-methoxybenzyl)-1-deoxy-3,4-O-isopropylidene-1-{4-[2-(trimethylsilyl)ethoxymethoxy]phenylthio}-β-D-galactopyranose 82 as a colorless oil: R_f 0.4 (25% EtOAc/hexane); ¹H NMR (CDCl₃, 270 MHz,) δ 7.50 (d, J = 8.6 Hz, 2H), 7.36 (d, J = 8.6 Hz, 2H), 7.24 (d, J = 9.6 Hz, 2H), 6.89 (m, 6H), 5.17 (s, 2H, SEM), 4.75 (d, J = 10.9 Hz, 1H, PMB), 4.62 (d, J = 10.9 Hz, 1H, PMB), 4.51 (d, J = 11.2 Hz, 1H, PMB), 4.49 (d, J = 9.5 Hz, 1H, H-1), 4.44 (d, J = 11.2 Hz, 1H, PMB), 4.22 (t, J = 5.6 Hz, 1H, H-3), 4.17 (dd, J = 5.6, 1.7 Hz, 1H, H-4), 3.83 (dt, J = 1.7, 6.0 Hz, 1H, H-5), 3.81 (s, 6H, 2X-OMe), 3.73 (m, 4H), 3.45 (dd, J = 5.6, 9.7 Hz, 1H, H-2), 1.41 (s, 3H, C-CH₃), 1.34 (s, 3H, C-CH₃), 0.94 (t, J = 8.4 Hz, 2H, CH₂-TMS), 0.01 (s, 9H, SiMe₃).

To a solution of 82 (53 mg, 0.082 mmol) in 4 mL of MeOH is added p-toluenesulfonic acid hydrate (3 mg, 0.016 mmol). The mixture is stirred at room temperature for 9 h, neutralized with pyridine (2 drops), concentrated, and purified by flash chromatography (60% EtOAc/hexane) to give 35 mg (81%) of 2,6-bis-O-(4-methoxybenzyl)-1-deoxy-1-(4-hydroxyphenylthio)-β-D-galactopyranose 83 as a colorless oil: R_f 0.4 (60% EtOAc/hexane); ¹H NMR (CDCl₃, 270 MHz) δ 7.46 (d, J = 8.6 Hz, 2H), 7.34 (d, J = 8.6 Hz, 2H), 7.24 (d, J = 8.6 Hz, 2H), 6.87 (m, 4H), 6.68 (d, J = 8.2 Hz, 2H), 5.65 (br s, 1H), 4.88 (d, J = 10.9 Hz, 1H, PMB), 4.63 (d, J = 10.9 Hz, 1H, PMB), 4.49 (s, 2H, PMB), 4.46 (d, J = 9.9 Hz, 1H, H-1), 3.99 (d, J = 2.3 Hz, 1H, H-4), 3.80 (s, 6H, 2X-OMe), 3.74 (d, J = 5.3 Hz, 2H), 3.56 (m, 2H), 3.53 (t, J = 8.9 Hz, 1H), 2.80 (br s, 1H), 2.50 (br s, 1H).

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To a solution of 83 (35 mg, 0.066 mmol) in 4 mL of
DMF is added K$_2$CO$_3$ (15 mg, 0.11 mmol) and 2-
(trimethylsilyl)ethyl bromoacetate (25 mg, 0.10 mmol).
The reaction is stirred at 45-50 °C for 3 h,
concentrated *in vacuo* and purified by flash
chromatography (60% EtOAc/hexane) to give 35 mg (89%)
of 2-(trimethylsilyl)ethyl 2-{4-[(2,6-bis-O-(4-
methoxybenzyl)-1-deoxy-β-D-galactopyranosyl)thio]-
phenoxy}acetate **84** as a colorless oil: R$_f$ 0.5 (60%
EtOAc/hexane); ^{1}H NMR (CDCl$_3$, 270 MHz) δ 7.53 (d, *J* =
8.6 Hz, 2H), 7.33 (d, *J* = 8.6 Hz, 2H), 7.23 (d, *J* = 8.6
Hz, 2H), 6.87 (m, 4H), 6.79 (d, *J* = 8.6 Hz, 2H), 4.87
(d, *J* = 10.6 Hz, 1H), 4.63 (d, *J* = 10.6 Hz, 1H), 4.56
(s, 2H), 4.49 (s, 2H), 4.48 (d, *J* = 8.9 Hz, 1H, H-1),
4.30 (m, 2H), 3.81 (s, 6H), 3.74 (dd, *J* = 2.0, 5.0 Hz,
1H), 3.57 (m, 2H), 3.53 (dd, *J* = 8.9, 8.9 Hz, 1H), 2.69
(br s, 1H), 2.40 (br s, 1H), 1.03 (m, 2H, CH$_2$-TMS),
0.01 (s, 9H, SiMe$_3$).

To a solution of **84** (141 mg, 0.205 mmol) in 10 mL
of CH$_2$Cl$_2$ at -78 °C is added N,N-diisopropylethylamine
(0.090 mL, 0.51 mmol), acetic anhydride (0.021 mL, 0.23
mmol) and DMAP (4 mg, 0.03 mmol). The solution is
stirred at -78 °C for 30 min, then diluted with 25 mL
of EtOAc and washed with saturated NH$_4$Cl (25 mL) and
saturated NaHCO$_3$ (25 mL). The aqueous layers are back-
extracted with EtOAc (25 mL). The organic layers are
combined, dried over Na$_2$SO$_4$, concentrated and purified
by flash chromatography (45% EtOAc/hexane) to give 125
mg (83%) of 2-(trimethylsilyl)ethyl 2-{4-[(3-O-acetyl-
2,6-bis-O-(4-methoxybenzyl)-1-deoxy-β-D-
galactopyranosyl)thio]phenoxy}acetate **85** as a colorless
oil: R$_f$ 0.5 (50% EtOAc/hexane); ^{1}H NMR (CDCl$_3$, 270 MHz)
δ 7.53 (d, *J* = 8.6 Hz, 2H), 7.24 (m, 4H), 6.87 (m, 4H),
6.79 (d, *J* = 8.9 Hz, 2H), 4.89 (dd, *J* = 2.6, 9.5 Hz,
1H, H-3), 4.78 (d, *J* = 10.5 Hz, 1H), 4.55 (m, 4H), 4.50
(s, 2H), 4.46 (d, *J* = 11.5 Hz, 1H), 4.30 (m, 2H), 4.18

(dd, J = 2.6, 3.4 Hz, 1H, H-4), 3.81 (s, 3H, OMe), 3.80
(s, 3H, OMe), 3.74 (m, 3H), 3.60 (t, J = 4.6 Hz, 1H),
2.91 (d, J = 3.4 Hz, 1H), 2.06 (s, 3H, OAc), 1.03 (m,
2H, CH$_2$-TMS), 0.04 (s, 9H, SiMe$_3$).

To a solution of **85** (1.30 g, 1.79 mmol) in 13 mL
of CH$_2$Cl$_2$ at -35 °C is added pyridine (0.072 mL, 8.93
mmol) followed by triflic anhydride (0.451 mL, 2.68
mmol). The reaction is allowed to warm slowly to 0 °C
and is then poured into saturated NaHCO$_3$ (50 mL),
extracted with CH$_2$Cl$_2$ (3 x 30 mL), dried over Na$_2$SO$_4$,
concentrated and purified by flash chromatography (25%
EtOAc/hexane) to give 1.10 g (71%) of 2-
(trimethylsilyl)ethyl 2-{4-[(3-O-acetyl-2,6-bis-O-(4-
methoxybenzyl)-1-deoxy-4-O-trifluoromethanesulfonyl-β-
D-galactopyranosyl)thio]phenoxy}acetate **86** as a
colorless oil: R$_f$ 0.5 (25% EtOAc/hexane); ^{1}H NMR
(CDCl$_3$, 270 MHz) δ 7.48 (d, J = 8.9 Hz, 2H), 7.24 (m,
4H), 6.84 (m, 6H), 5.33 (d, J = 2.6 Hz, 1H, H-4), 5.00
(dd, J = 2.6, 9.6 Hz, 1H, H-3), 4.76 (d, J = 10.9 Hz,
1H), 4.40 (m, 5H), 4.31 (m, 3H), 3.81 (m, 1H), 3.81(s,
6H, 2X-OMe), 3.67 (ddd, J = 2.3, 9.6, 9.6 Hz, 1H), 3.53
(dd, J = 8.7, 8.7 Hz, 1H), 2.03 (s, 3H, OAc), 1.04 (m,
2H, CH$_2$-TMS), 0.01 (s, 9H, SiMe$_3$).

To a solution of **86** (1.10 g, 1.28 mmol) in 15 mL
of DMF is added NaN$_3$ (831 mg, 12.8 mmol). The reaction
is stirred at room temperature for 1.5 h and then
poured into water (100 mL), extracted with CH$_2$Cl$_2$ (3 x
50 mL), dried over Na$_2$SO$_4$, concentrated and purified by
flash chromatography (25% EtOAc/hexane) to give 0.96 g
(99%) of 2-(trimethylsilyl)ethyl 2-{4-[(3-O-acetyl-4-
azido-2,6-bis-O-(4-methoxybenzyl)-1,4-dideoxy-β-D-
glucopyranosyl)thio]phenoxy}acetate **87** as a colorless
oil: R$_f$ 0.5 (25% EtOAc/hexane); ^{1}H NMR (CDCl$_3$, 270
MHz,) δ 7.51 (d, J = 8.9 Hz, 2H), 7.23 (m, 4H), 6.91
(d, J = 8.9 Hz, 2H), 6.86 (d, J = 6.6 Hz, 2H), 6.79 (d,
J = 8.9 Hz, 2H), 5.13 (dd, J = 9.2, 9.9 Hz, 1H, H-3),

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4.77 (d, J = 10.9 Hz, 1H), 4.51 (m, 6H), 4.30 (m, 2H),
3.82 (s, 3H, OMe), 3.80 (s, 3H, OMe), 3.68 (m, 3H),
3.39 (dd, J = 9.4, 9.4 Hz, 1H), 3.31 (m, 1H), 2.00 (s,
3H, OAc), 1.04 (m, 2H, CH_2-TMS), 0.05 (s, 9H, $SiMe_3$).

    To a solution of **87** (370 mg, 0.49 mmol) in 10 mL
of THF is added tetrabutylammonium fluoride solution
(1M in THF, 2.46 mL, 2.46 mmol). The reaction is
stirred at room temperature for 30 min and then diluted
with EtOAc (25 mL) and washed with 0.5 M HCl (20 mL)
and saturated NaCl (20 mL). The aqueous layer is back-
extracted with EtOAc (25 mL) and the organic layers are
combined, dried over Na_2SO_4, concentrated, and purified
by flash chromatography (0.3% AcOH, 10% MeOH, in EtOAc)
to give 250 mg (78%) of 2-{4-[(3-O-acetyl-4-azido-2,6-
bis-O-(4-methoxybenzyl)-1,4-dideoxy-β-D-
glucopyranosyl)thio]phenoxy}acetic acid **88** as a white
solid: R_f 0.4 (0.3% AcOH, 10% MeOH/EtOAc); ^{1}H NMR
($CDCl_3$, 300 MHz) δ 7.51 (d, J = 8.8 Hz, 2H), 7.24 (m,
4H), 6.91 (d, J = 8.8 Hz, 2H), 6.86 (d, J = 8.4 Hz,
2H), 6.76 (d, J = 8.8 Hz, 2H), 5.14 (dd, J = 9.2, 9.2
Hz, 1H, H-3), 4.76 (d, J = 9.6 Hz, 1H), 4.62 (s, 2H),
4.50 (m, 4H), 3.83 (s, 3H, OMe), 3.80 (s, 3H, OMe),
3.73 (m, 2H), 3.64 (dd, J = 9.9, 9.9 Hz, 1H), 3.39 (dd,
J = 9.2, 9.5 Hz, 1H), 3.32 (m, 1H), 2.00 (s, 3H, OAc);
^{13}C NMR (C_6D_6, 126 MHz) δ 170.4, 160.6, 160.5, 159.5,
135.6, 131.6, 125.5, 116.5, 114.8, 114.7, 88.3, 79.2,
78.4, 76.8, 75.1, 73.9, 70.0, 66.2, 61.7, 55.9, 30.9,
30.6, 30.5, 30.3, 30.0, 29.9, 29.7, 21.3; FABMS
$C_{32}H_{35}O_{10}N_3S$ calcd 676.1940, found 676.1960

7.30. 2-{4-[(3-O-acetyl-4,6-O-benzylidene-1-deoxy-2-O-(4-methoxybenzyl)-β-D-galactopyranosyl)thio]phenoxy}acetic acid (95)

    To a solution of **81**, prepared as above (139
mg, 0.303 mmol) and 2,6-di-t-butyl-4-methyl pyridine
(187 mg, 0.91 mmol) in 5 mL CH_2Cl_2 are added

chlorotriphenylmethane (101 mg, 0.364 mmol) and silver trifluoromethanesulfonate (78 mg, 0.30 mmol). The reaction mixture is stirred at room temperature for 45 min and then is filtered though celite and washed with 10 mL of aqueous NaHCO$_3$. The aqueous solution is extracted with CH$_2$Cl$_2$ (2 x 10 mL) and the organic layers are combined and dried over Na$_2$SO$_4$, filtered and concentrated. The product is purified by flash chromatography (25% EtOAc/hexane) to give 171 mg (81%) of 1-deoxy-3,4-O-isopropylidene-1-{4-[2-(trimethylsilyl)ethoxymethoxy]phenylthio}-6-O-triphenylmethyl-β-D-galactopyranose 89 as white solid: R$_f$ 0.2 (25% EtOAc/hexane); ¹H NMR (CDCl$_3$, 300 MHz) δ 7.53-7.40 (m, 8H), 7.31-7.21 (m, 9H), 6.95 (d, J = 8.5Hz, 2H), 5.19 (s, 2H), 4.29 (d, J = 10.2Hz, 1H, H-1), 4.14 (dd, J = 5.6, 2.0Hz, 1H, H-4), 4.02 (dd, J = 6.9, 5.6Hz, 1H, H-3), 3.73 (m, 3H), 3.56 (dd, J = 9.6, 6.9Hz, 1H, H-6), 3.48 (ddd, J = 8.9, 6.9, 2.0Hz, 1H, H-2), 3.36 (dd, J = 9.6, 5.3Hz, 1H, H-6), 2.37 (d, J = 2.0Hz, 1H, OH), 1.37 (s, 3H), 1.31 (s, 3H), 0.96 (t, J = 7.2Hz, 2H), 0.00 (s, 9H).

To a solution of 89 (365 mg, 0.521 mmol) and tetrabutylammonium iodide (770 mg, 2.08 mmol) in 5 mL of DMF is added 4-methoxybenzyl chloride (0.422 mL, 4.17 mmol) and sodium hydride (19 mg, 0.782 mmol). The reaction is stirred at room temperature for one hour and then diluted with 50 mL of CH$_2$Cl$_2$, washed with brine (3 x 20 mL), dried over Na$_2$SO$_4$, filtered, and concentrated to afford a white solid which is purified by flash chromatography (12% EtOAc/hexane) to give 399 mg (93%) of 1-deoxy-3,4-O-isopropylidene-2-O-(4-methoxybenzyl)-1-{4-[2-(trimethylsilyl)-ethoxymethoxy]phenylthio}-6-O-triphenylmethyl-β-D-galactopyranose 90 as a white foam: R$_f$ 0.25 (12% EtOAc/hexane); ¹H NMR (CDCl$_3$, 270 MHz) δ 7.51 (d, J = 8.5Hz, 2H), 7.48-7.45 (m, 6H), 7.34-7.20 (m, 11H),

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6.91-6.87 (m, 4H), 5.16 (s, 2H), 4.76 (d, J = 10.9Hz,
1H), 4.62 (d, J = 10.9Hz, 1H), 4.40 (d, J = 9.9Hz, 1H,
H-1), 4.19-4.10 (m, 2H), 3.80-3.70 (m, 5H), 3.58-3.53
(m, 2H), 3.45-3.39 (dd, J = 6.3, 9.6Hz, 1H, H-6), 3.36-
3.32 (m, 1H), 1.36 (s, 3H), 1.32 (s, 3H), 0.95 (t, J =
8.2Hz, 2H), 0.00 (s, 9H).

To a solution of **90** (399 mg, 0.486 mmol) in 15 mL
of methanol is added p-toluenesulfonic acid hydrate (69
mg, 0.365 mmol). The reaction mixture is stirred at
room temperature for 4.5 h and then quenched by adding
solid NaHCO$_3$ and then concentrated and purified by
flash chromatography (3% methanol/EtOAc) to give 125 mg
(65%) of 1-deoxy-1-(4-hydroxyphenylthio)-2-O-(4-
methoxybenzyl)-β-D-galactopyranose **91** as a white solid:
R$_f$ 0.5 (10% methanol/EtOAc); ^{1}H NMR (CD$_3$OD, 270 MHz) δ
7.42-7.38 (m, 4H), 6.88 (d, J = 8.9Hz, 2H), 6.71 (d, J
= 8.6Hz, 2H), 4.74 (s, 2H), 4.42 (d, J = 9.5Hz, 1H, H-
1), 3.86 (d, J = 2.6Hz, 1H), 3.79 (s, 3H, OCH$_3$), 3.77-
3.70 (m, 2H), 3.61-3.45 (m, 3H).

To a solution of **91** (717 mg, 1.89 mmol) in 100 mL
DMF is added benzaldehyde dimethyl acetal (1.4 mL, 9.12
mmol) and p-toluenesulfonic acid hydrate (36 mg, 0.189
mmol). The reaction mixture is stirred overnight at
room temperature, quenched by adding solid sodium
bicarbonate then concentrated *in vacuo*. The residue is
purified by flash chromatography (60% EtOAc/hexane) to
give 400 mg (43%) of 4,6-O-benzylidene-1-deoxy-1-(4-
hydroxyphenylthio)-2-O-(4-methoxybenzyl)-β-D-
galactopyranose **92** as a white solid: R$_f$ 0.2 (60%
EtOAc/hexane); ^{1}H NMR (CDCl$_3$, 270 MHz) δ 7.60 (d, J =
8.8Hz, 2H), 7.47-7.33 (m, 7H), 6.88 (d, J = 8.4Hz, 2H),
6.71 (d, J = 8.8Hz, 2H), 5.53 (s, 1H), 5.17 (s, 1H),
4.75 (d, J = 10.3Hz, 1H), 4.64 (d, J = 10.3Hz, 1H),
4.49 (d, J = 9.3Hz, 1H, H-1), 4.37 (dd, J = 12.4,
1.7Hz, 1H, H-6), 4.20 (d, J = 3.6Hz, 1H, H-4), 4.02
(dd, J = 12.4, 1.4Hz, 1H, H-6), 3.80 (s, 3H, OCH$_3$),

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3.76 (td, J = 3.8, 3.7Hz, 1H, H-3), 3.56 (t, J = 9.1Hz,
1H, H-2), 3.49 (m, 1H, H-5), 2.43 (d, J = 8.4Hz, 1H).

To a solution of **92** (400 mg, 0.806 mmol) in 80 mL
of dry DMF is added 2-(trimethylsilyl)ethyl
bromoacetate (478 mg, 2 mmol) followed by K_2CO_3 (111
mg, 0.806 mmol). The reaction mixture is stirred at 60
°C for 4 hr and then allowed to cool. The solution is
diluted with 150 mL of EtOAc and washed with brine (3 x
40 ml), dried over Na_2SO_4, filtered, concentrated and
purified by flash chromatography (50% EtOAc/hexane) to
give 260 mg (53%) of 2-(trimethylsilyl)ethyl 2-{4-
[(4,6-O-benzylidene-1-deoxy-2-O-(4-methoxybenzyl)-β-D-
galactopyranosyl)thio]phenoxy}acetate **93** as a white
solid: R_f 0.3 (50% EtOAc/hexane); ^1H NMR ($CDCl_3$, 270
MHz) δ 7.6 (d, J = 8.8Hz, 2H), 7.45-7.25 (m, 7H), 6.82
(d, J = 8.5Hz, 2H), 6.71 (d, J = 8.8Hz, 2H), 5.49 (s,
1H), 4.68 (d, J = 10.3Hz, 1H), 4.57 (d, J = 9.9Hz, 1H),
4.49 (s, 2H), 4.46 (d, J = 9.5Hz, 1H, H-1), 4.32 (dd, J
= 12.5, 1.5Hz, 1H, H-6), 4.28-4.22 (m, 2H), 4.16 (d, J
= 3.3Hz, 1H, H-4), 3.97 (dd, J = 12.5, 1.5Hz, 1H, H-6),
3.75 (s, 3H, OCH_3), 3.71 (td, J = 8.4, 3.3Hz, 1H, H-3),
3.52 (t, J = 9.1Hz, 1H, H-2), 3.44 (m, 1H, H-5), 2.35
(d, J = 8.4Hz, 1H, OH), 0.989-0.917 (m, 2H), 0.0 (s,
9H).

To a solution of **93** (260 mg; 0.41 mmol) in 50 mL
of CH_2Cl_2 is added pyridine (0.140 mL, 1.64 mmol) and
acetic anhydride (0.078 mL, 0.82 mmol). The reaction
mixture is stirred at room temperature for 2 hr and
quenched by adding 1 mL of methanol. The reaction
mixture is washed with 20 mL of $NaHCO_3$ solution and the
aqueous layer is extracted with CH_2Cl_2 (2 x 40 mL).
The organic layers are combined, dried over Na_2SO_4,
filtered, concentrated and purified by flash
chromatography (50% EtOAc/hexane) to give 252 mg (91%)
of 2-(trimethylsilyl)ethyl 2-{4-[(3-O-acetyl-4,6-O-
benzylidene-1-deoxy-2-O-(4-methoxybenzyl)-β-D-

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galactopyranosyl)thio]phenoxy}acetate **94** as a white solid: R$_f$ 0.4 (50% EtOAc/hexane); ^{1}H NMR (CDCl$_3$, 270 MHz) δ 7.63 (d, J = 8.9Hz, 2H), 7.48-7.24 (m, 7H), 6.86 (d, J = 8.6Hz, 2H), 6.72 (d, J = 8.9Hz, 2H), 5.49 (s, 1H), 4.92 (dd, J = 9.9, 3.3Hz, 1H, H-3), 4.70 (d, J = 10.2Hz, 1H), 4.58 (d, J = 9.6Hz, 1H, H-1), 4.51 (s, 2H), 4.46 (d, J = 10.2Hz, 1H), 4.38-4.27 (m, 4H), 4.00 (bd, J = 12.2Hz, 1H, H-6), 3.84 (t, J = 9.5Hz, 1H, H-2), 3.79 (s, 3H, OCH$_3$), 3.55 (m, 1H, H-5), 2.03 (s, 3H), 1.07-1.00 (m, 2H), 0.05 (s, 9H).

To a solution of **94** (252 mg, 0.365 mmol) in 2 mL of THF is added tetrabutylammonium fluoride solution (1.0M in THF, 0.380 ml, 0.380 mmol) at room temperature. The reaction mixture is stirred for 5 mins and then directly loaded to a silica gel column and purified by flash chromatography (0.1% AcOH,10% methanol, in EtOAc) to give 196 mg (91%) of the title compound **95** as a white solid: R$_f$ 0.1 (0.1% AcOH,10% methanol/EtOAc); ^{1}H NMR (CDCl$_3$, 270 MHz) δ 9.72 (bs, 1H), 7.57 (d, J = 8.5Hz, 2H), 7.47-7.29 (m, 5H), 7.26 (d, J = 8.5Hz, 2H), 6.86 (d, J = 8.4Hz, 2H), 6.83 (d, J = 8.4Hz, 2H), 5.48 (s, 1H), 4.92 (dd, J = 9.5, 3.3Hz, 1H, H-3), 4.73 (d, J = 11.2Hz, 1H), 4.57 (d, J = 9.5Hz, 1H, H-1), 4.50-4.38 (m, 3H), 4.37-4.31 (m, 2H), 4.00 (bd, J = 12Hz, 1H, H-6), 3.85 (t, J = 9.5Hz, 1H, H-2), 3.80 (s, 3H, OCH$_3$), 3.52 (m, 1H, H-5), 2.03 (s, 3H); ^{13}C NMR (CDCl$_3$, 68 MHz) δ 172.3, 170.7, 159.5, 157.6, 138.0, 135.3, 130.5, 129.5, 129.1, 128.2, 126.5, 124.8, 115.3, 113.9, 100.8, 86.9, 75.7, 75.0, 74.0, 73.8, 69.5, 69.3, 65.0, 55.4, 21.1.

7.31   Attachment Of A Glycosyl Acceptor To A Resin Support

A number of glycosyl acceptors, to be used as nucleophiles for coupling to the hexose derivatives of the invention, are coupled to a solid support by the

following general method: TentaGel S NH$_2$ resin (0.500
g) is suspended in N-methylpyrrolidinone (NMP, 15 mL),
and to this mixture is added acid 64 (0.115 g, 0.230
mmol), diisopropylethylamine (0.22 g, 1.3 mmol), and
HOBT/HBTU solution (0.45 M in DMF, 2.2 g, 0.93 mmol).
The reaction mixture is then shaken for 2-5 h until the
resin gives a negative Kaiser test. The resin is
washed with CH$_2$Cl$_2$ (3 x 15 mL, 5 min), NMP (3 x 15 mL,
5 min), and DMF (3 x 15 mL, 5 min).

A solution of hydrazine in DMF (1:7 v/v, 24 mL) is
added to the resin. The mixture is shaken for 9 h or
until acetate hydrolysis is shown to be complete by IR
analysis (KBr pellet). The resin is then washed with
DMF (3 x 15 mL, 5 min), H$_2$O (3 x 15 mL, 5 min),
methanol (3 x 15 mL, 5 min) and CH$_2$Cl$_2$ (3 x 15 mL, 5
min).

In the present embodiment, six glycosyl acceptors
(glycosylated acids 64, 66, 76, 77, 88 and 95) are
attached to six separate batches of resin (e.g.,
TentaGel) and deprotected using the procedure described
above. Each batch of support-bound glycosyl resin can
then be used in the subsequent glycosylation reaction
after suspension in 15 mL of CH$_2$Cl$_2$, shaking for 15 min
and drying on the lyophilizer for 12 h.

7.32. Procedure For Solid Phase Glycosylation

In a typical procedure, a predetermined
portion (0.225 g) of each batch of resin is placed in a
reaction vessel equipped with a glass-fritted bottom,
suspended in 5 mL of CH$_2$Cl$_2$ and agitated by slowly
bubbling argon through the glass frit for 10 min. The
1-sulfinyl hexose derivative 33 (0.145 g, 0.270 mmol)
and 2,6-di-tert-butyl-4-methylpyridine (0.111 g, 0.540
mmol) are dissolved in toluene (10 mL). The toluene is
subsequently removed in vacuo to remove any water that
may be present in solution. The dissolution and drying

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step is repeated at least once more. The residue is
then dried under vacuum for 1 h. Afterwards, the
sulfoxide and base are dissolved in CH_2Cl_2 (10 mL) and
added to the resin sample, e.g., the resin sample
bearing glycosyl acceptor **64**. The suspension is then
cooled to -65 °C, and a solution of
trifluoromethanesulfonic anhydride (23 μL, 0.13 mmol)
in 1 mL of CH_2Cl_2 is added dropwise over 10 min. The
reaction mixture is allowed to warm to 0 °C over 1-2 h,
quenched using saturated aqueous $NaHCO_3$ (10 mL) and
agitated for 10 min. The resin is then washed
sequentially with 10 mL portions (3 x 10 mL, 5 min for
each portion) of the following solvents: $NaHCO_3$, H_2O,
methanol, diethyl ether, CH_2Cl_2 and toluene. The resin
is dried on the lyophilizer (in vacuo) for 12 h and
resubjected to the glycosylation reaction conditions
for a second time to ensure complete reaction.

The stereoselectivity of the glycosylation
reaction is established by cleavage of the disaccharide
from the resin using mercuric trifluoroacetate (2.0
mg), in methylene chloride (0.5 mL) and shaking for 30
seconds. The $Hg(OCOCF_3)_2$ treatment causes the
hydrolytic cleavage of the thioacetal group. The
resulting lactol is then compared with an authentic
disaccharide, independently synthesized. The desired
disaccharide is obtained in greater than 9:1 alpha:beta
selectivity as judged by TLC (40% ethyl acetate in
petroleum ether, Rf 0.3) and HPLC analysis.

Glycosylation reactions using the hexose
derivatives **8**, **11**, **D-25**, **L-25**, **30** and **33**, with any of
the six resin samples obtained previously provide
comparable stereoselectivities of at least bout 9:1,
perhaps greater than 10:1.

Thus, using the above-described procedure, the
twelve resin samples are glycosylated with the 1-
sulfinyl hexose derivatives **5**, **11**, **13**, **D-25**, **L-25**, **33**,

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37, 41, D-45, L-45, 51 and 53. All 12 portions of the resin are then combined, suspended in 15 mL of CH_2Cl_2, shaken for 15 min and dried on the lyophilizer for 12 h.

Other embodiments should be apparent to those of ordinary skill in view of the detailed disclosure provided herein, which embodiments would nonetheless fall within the scope and spirit of the present invention. Hence, the preceding preferred embodiments should not be construed as limiting the invention in any way.

WHAT IS CLAIMED IS:

1.   A hexose of the formula
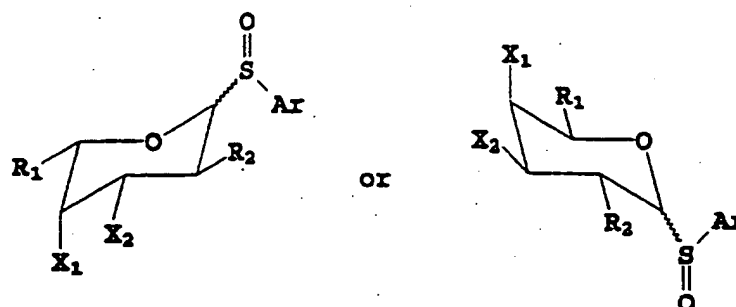
in which R_1 and R_2 may be the same or different and
each represents a substituent comprising one or more of
at least one of the elements hydrogen, carbon,
nitrogen, oxygen, sulfur, or phosphorus; Ar of the -
SOAr group represents an aromatic group; and X_1 and X_2
may be the same or different and together with the
hexose carbon atoms to which they are attached form a
cyclic structure.

2.   The hexose of claim 1 in which R_1
represents a lower alkyl group or a protected or
unprotected hydroxymethylene group.

3.   The hexose of claim 1 in which R_2
represents a protected or unprotected hydroxyl group, a
substituted or unsubstituted amine group, or an azide
group.

4.   The hexose of claim 1 in which Ar
represents a substituted or unsubstituted phenyl group.

5.   The hexose of claim 1 in which X_1 and X_2
together with the hexose carbon atoms to which they are
attached form a five-membered ring.

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6.   The hexose of claim 1 in which X_1 and X_2 together with the hexose carbon atoms to which they are attached form a cyclic carbonate.

7.   The hexose of claim 1 in which X_1 and X_2 together with the hexose carbon atoms to which they are attached form a cyclic ketal or cyclic acetal.

8.   A method of making a compound having an α- (1,2-cis)-glycosidic linkage comprising:

        (a) providing a glycosyl donor of the formula
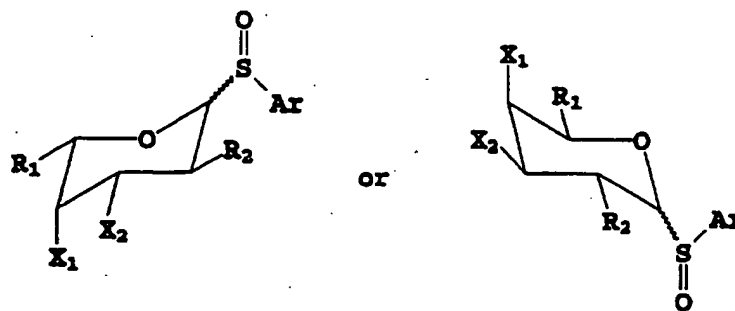
in which R_1 and R_2 may be the same or different and each represents a substituent comprising one or more of at least one of the elements hydrogen, carbon, nitrogen, oxygen, sulfur, or phosphorus; Ar of the - SOAr group represents an aromatic group; and X_1 and X_2 may be the same or different and together with the hexose carbon atoms to which they are attached form a cyclic structure; and

        (b) contacting said glycosyl donor with a compound having a nucleophilic group capable of displacing the -SOAr group.

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9.   The method of claim 8 which further comprises activating the -SOAr group to render it more susceptible to nucleophilic attack.

10.   The method of claim 9 in which said activating step comprises contacting said glycosyl donor with an organic acid or anhydride.

11.   The method of claim 8 in which said compound is bound to a solid support.

12.   The method of claim 8 which said compound includes an α-(1,6)-, α-(1,4)-, or α-(1,3)-disaccharide linkage.
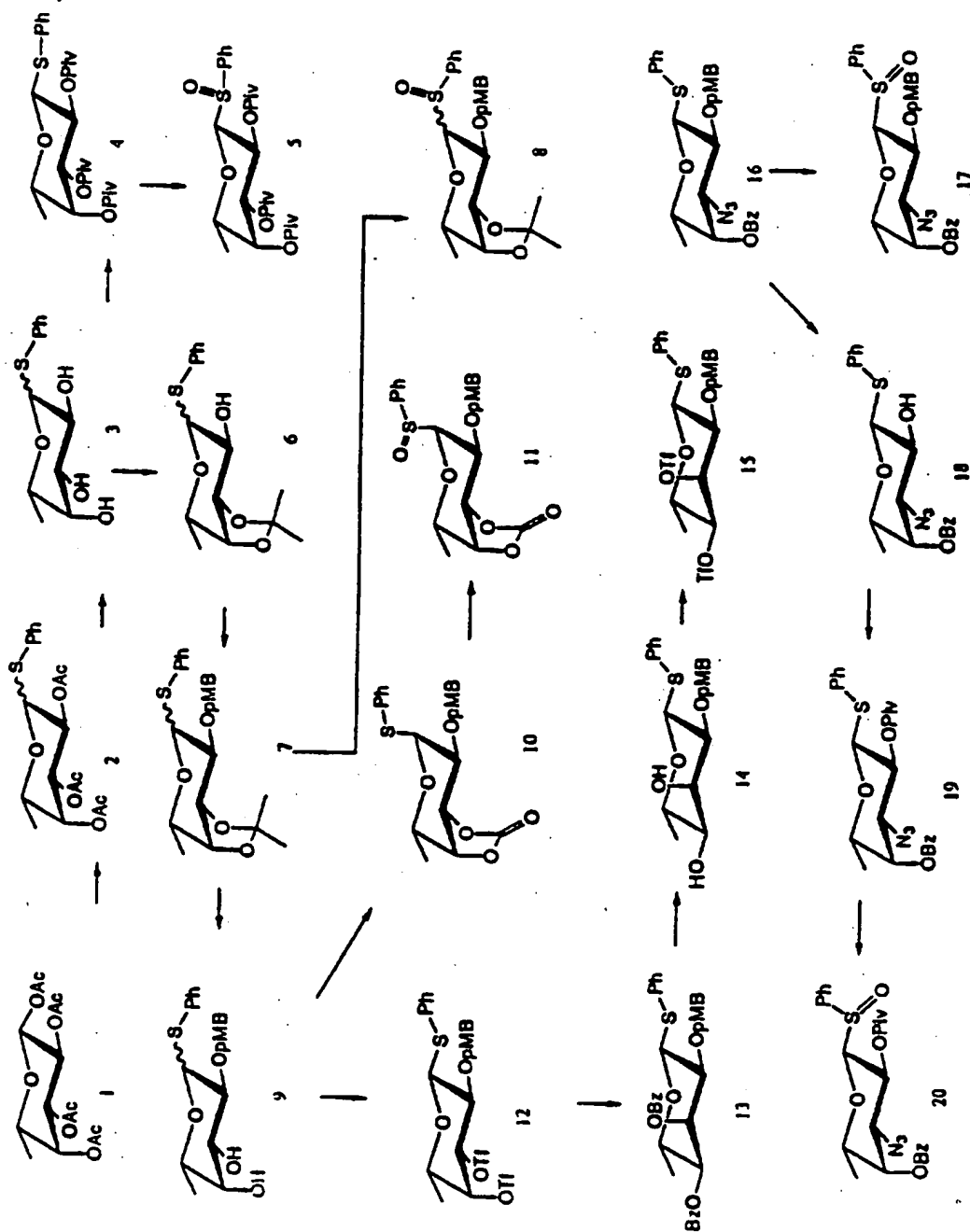
Figure 1
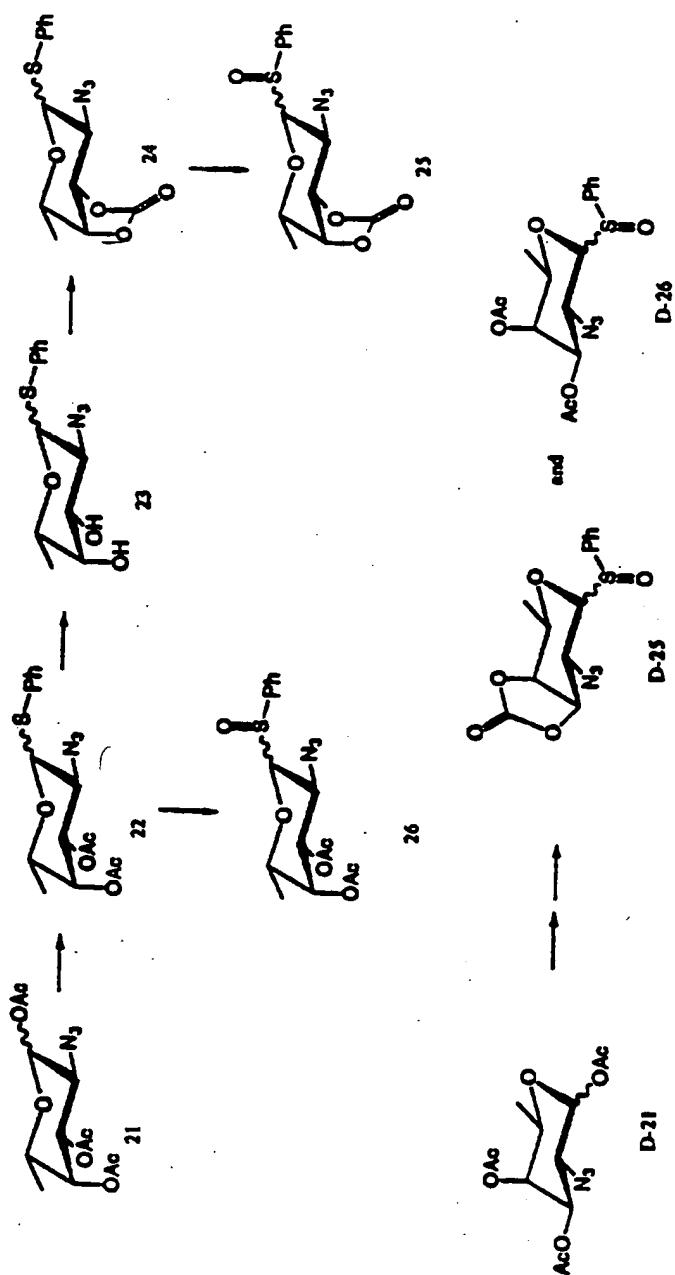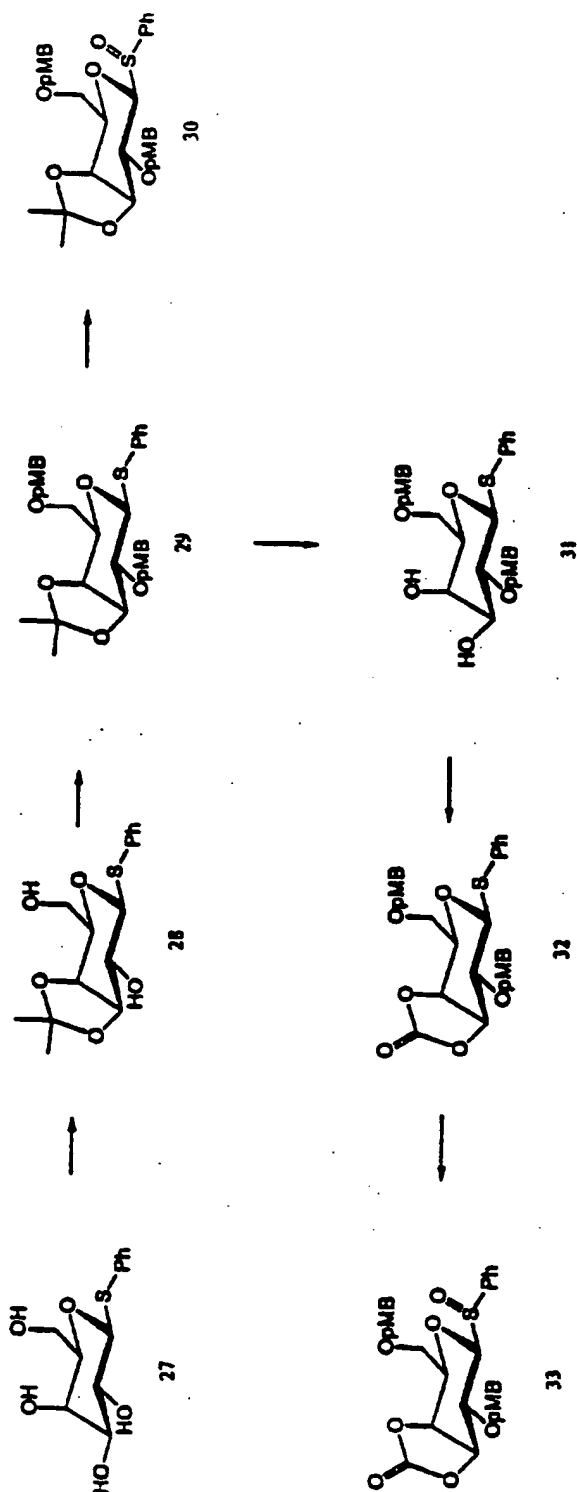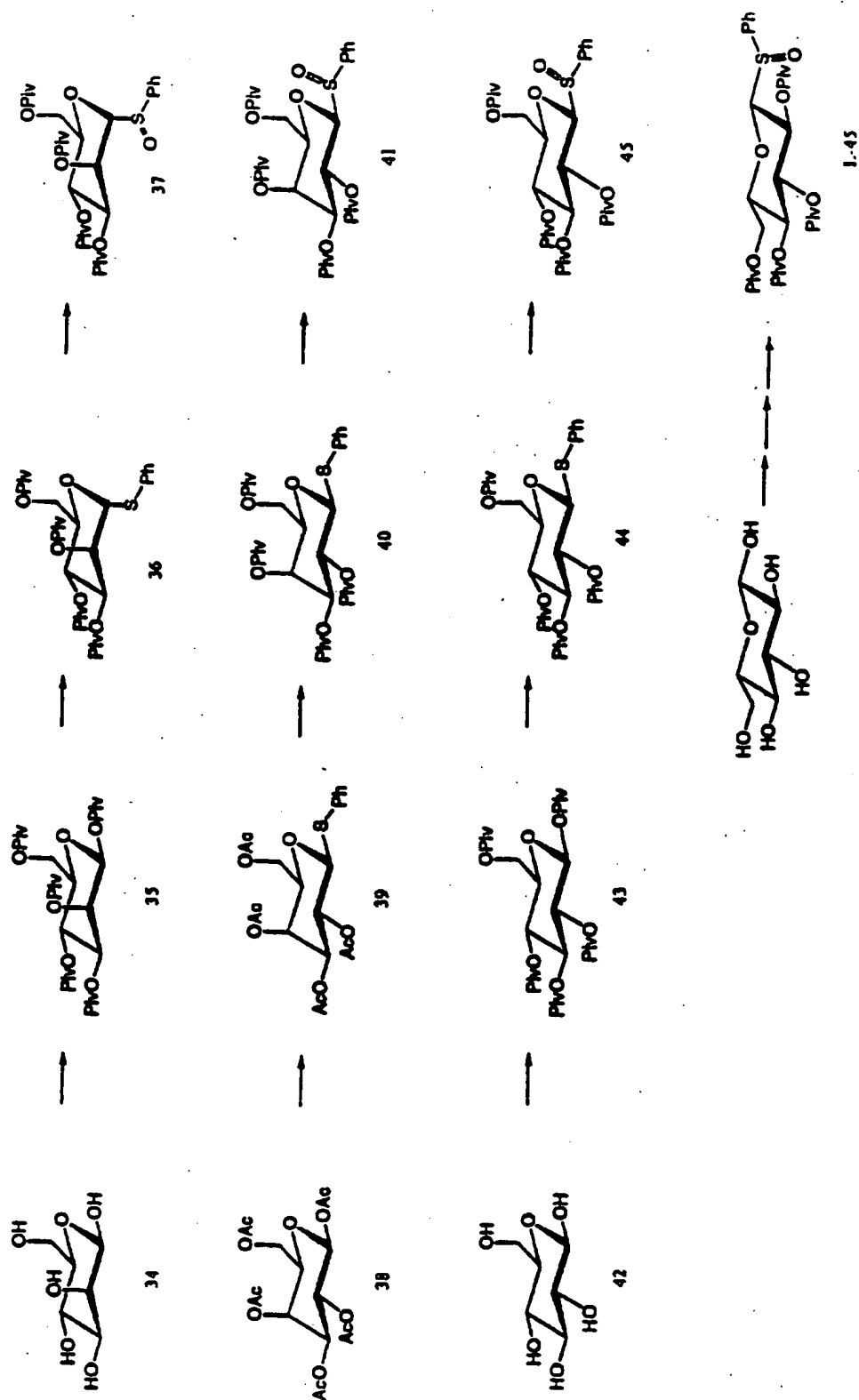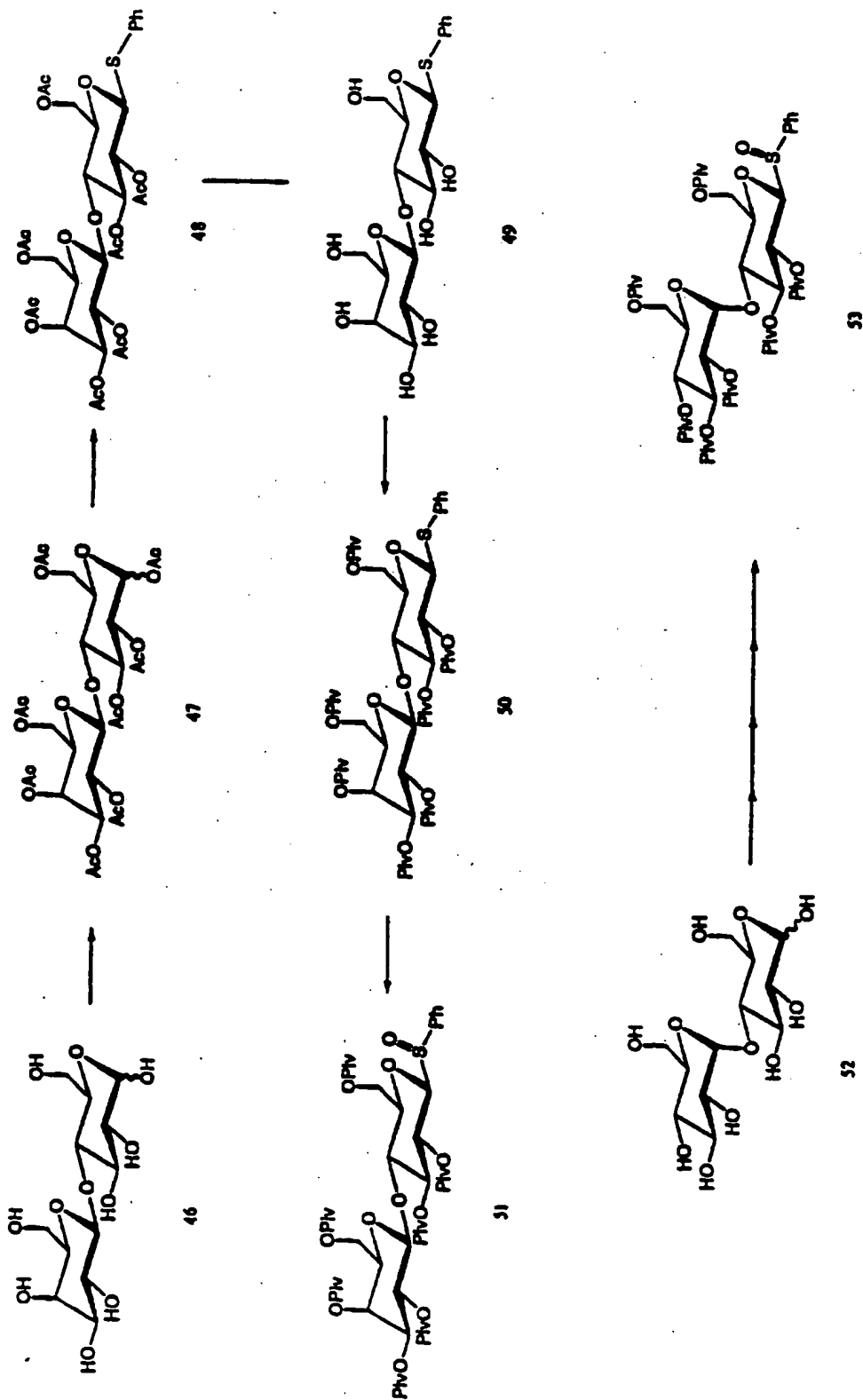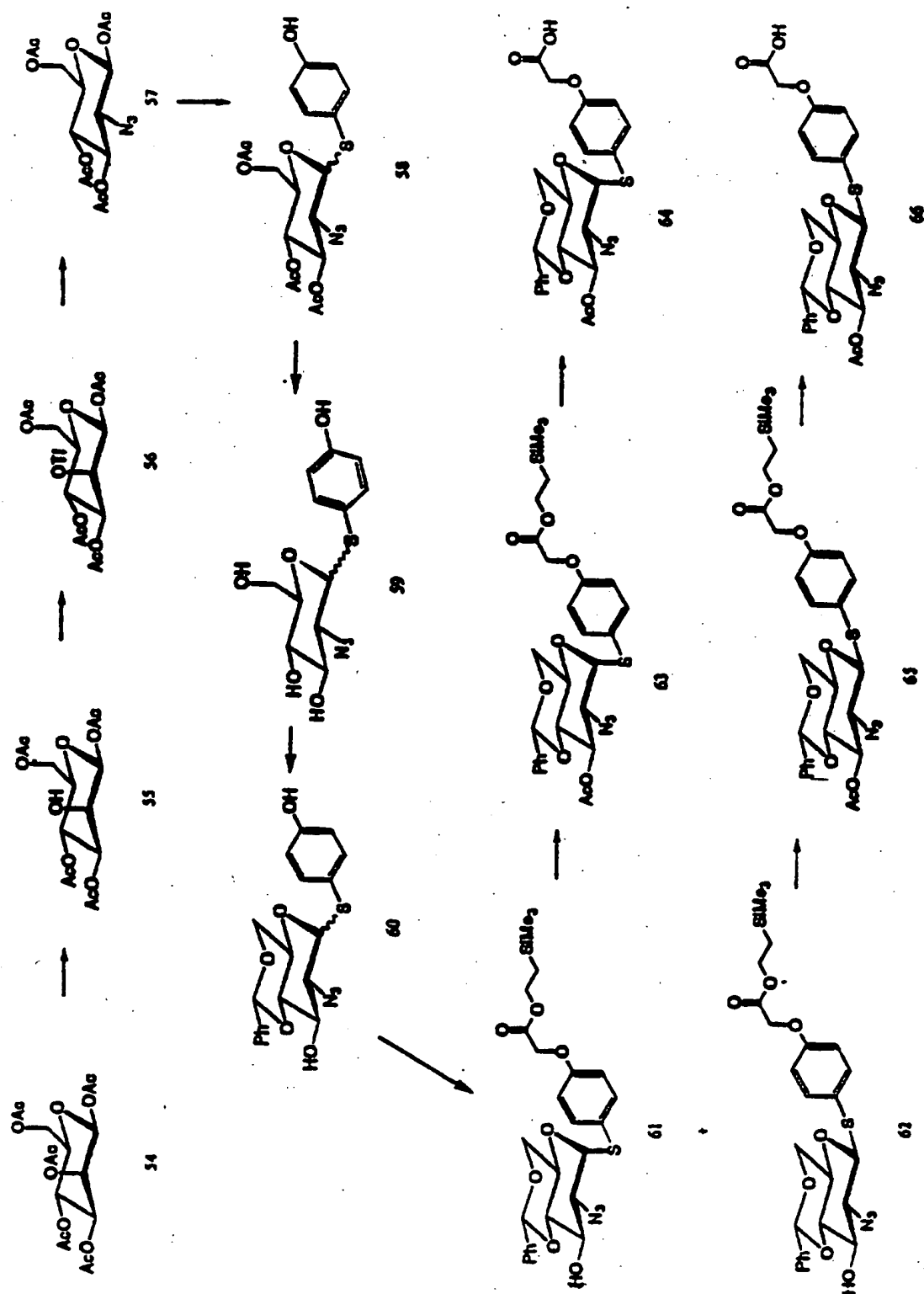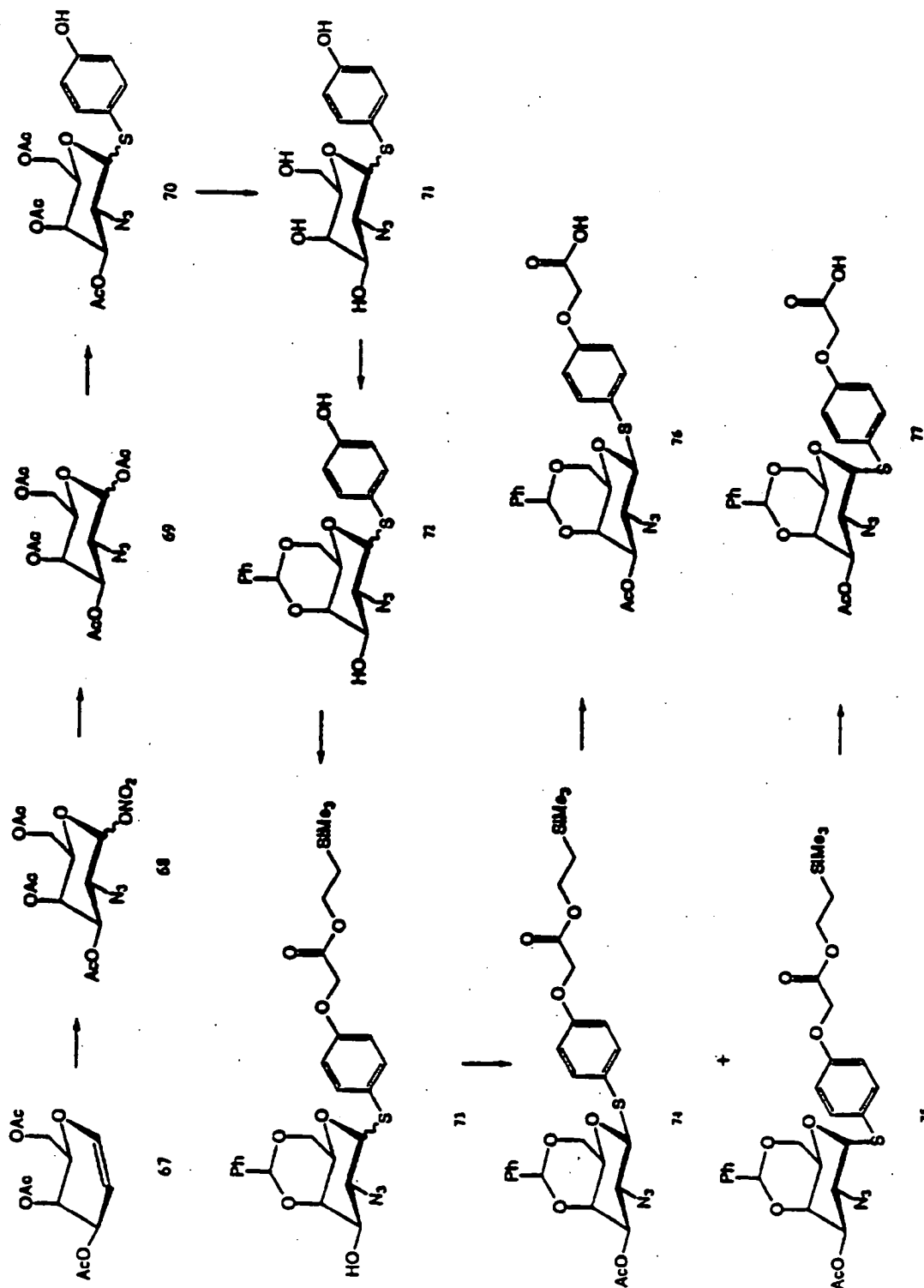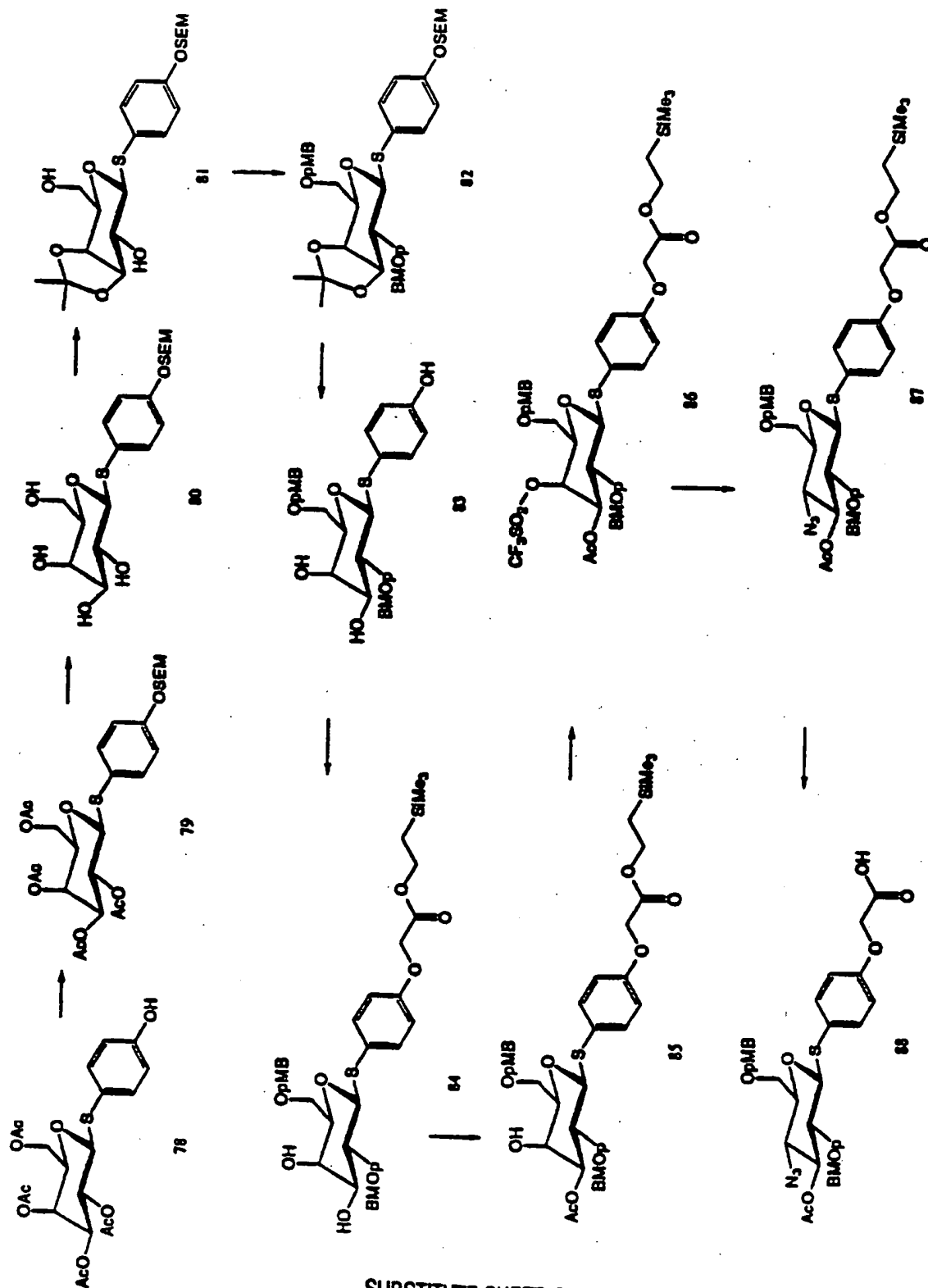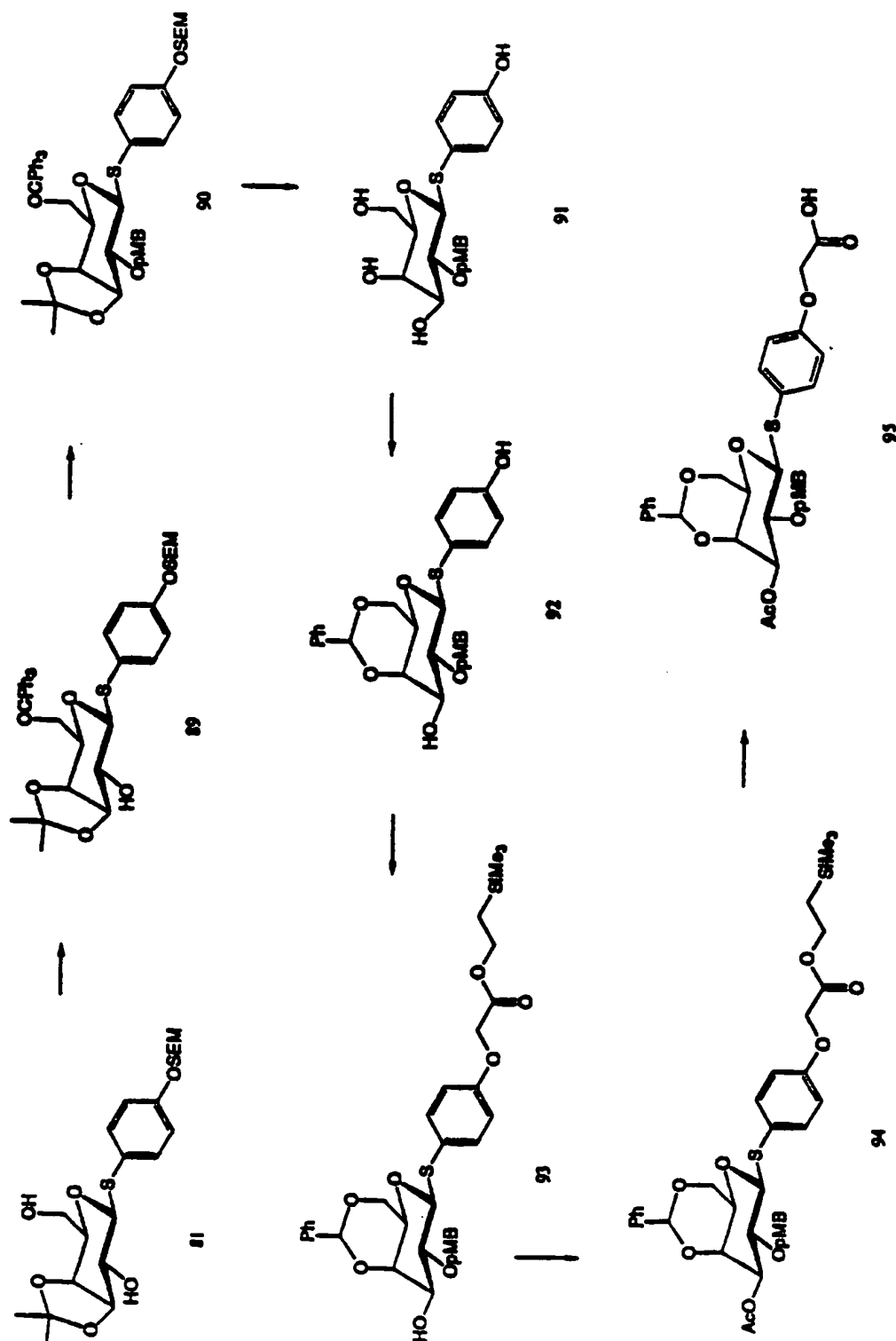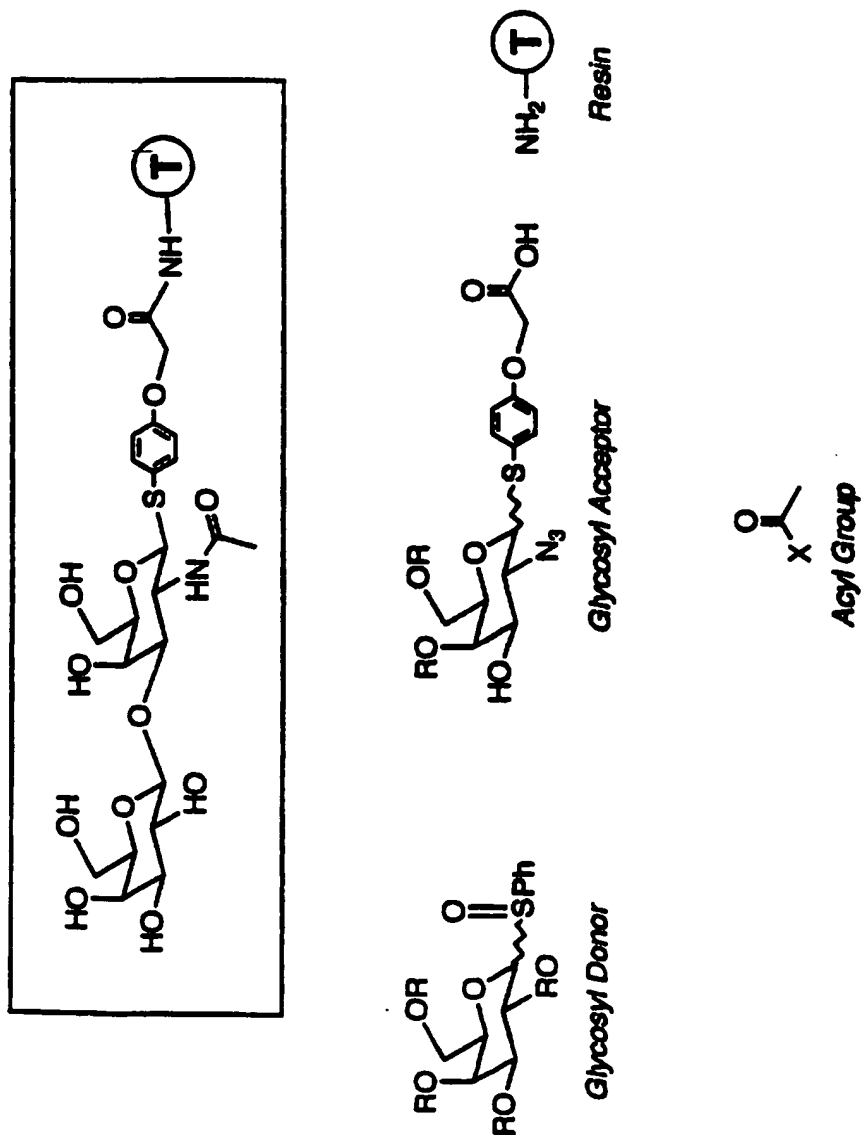
Figure 2

Figure 3

Figure 4

Figure 5

Figure 6

Figure 7

Figure 8

Figure 9

Figure 10

A. CLASSIFICATION OF SUBJECT MATTER
IPC(6) :C07G 3/00; C07H 1/00, 5/08, 5/10
US CL : 536/4.1, 122, 124
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
Minimum documentation searched (classification system followed by classification symbols)
U.S. : 536/4.1, 122, 124

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
APS, CAS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- A	ALONSO et al. A New Promoter System for the Sulfoxide Glycosylation Reaction. Tetrahedron Letters. 26 February 1996, Vol. 37, No. 9, pages 1477-1480, especially pages 1477 and 1478.	1-5, 7-10, 12 ----------- 6, 11

☐ Further documents are listed in the continuation of Box C.   ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
01 JULY 1997	2 4 JUL 1997

Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer EVERETT WHITE Telephone No. (703) 308-1235

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